VOL. 17 NO. 1 JANUARY, 1960

BRITISH JOURNAL OF INDUSTRIAL MEDICINE

EDITOR
L. G. NORMAN

ASSISTANT EDITORS
J. M. BARNES J. C. GILSON

CONTENTS

	PAGE
A Clinical and Environmental Study of Byssinosis in the Lancashire Cotton Industry. S. A. ROACH and R. S. F. SCHILLING	1
A Survey of Small Factories. MARGOT JEFFERYS and C. H. WOOD	10
Studies on the Nature of Silicosis: A Suggested Mechanism of Fibrogenesis. P. F. HOLT and C. W. WENT	25
Changes in the Lung Lipids of Rabbits and Guinea-pigs Exposed to the Inhalation of Silica Dust. G. S. MARKS and L. W. MARASAS	31
Drug Treatment of Experimental Silicosis. DINAH M. JAMES, T. G. MORRIS, and J. MARKS	36
A Comparison of the Emotional Stability of Coal-miners and Railwaymen. JUDITH S. LION	41
The Development of Rotary Nystagmus in the Cat as a Function of Age. N. E. LOVELESS	46
A Study of Heat Stress in Extremely Hot Environments, and the Infra-red Reflectance of Some Potential Shielding Materials. CHARLES E. LEWIS, RICHARD F. SCHERBERGER, and FRANKLIN A. MILLER	52
Excretion of Trichloroethylene Metabolites in Human Urine. B. SOUČEK and D. VLACHOVÁ	60
Ecological Considerations on Nickel Dermatitis. POUL V. MARCUSSEN	65
Renal Lesions in Experimental Cadmium Poisoning. J. A. BONNELL, J. H. ROSS, and E. KING	69
Two New Medical Centres	81
Book Reviews	82

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) £3. U.S.A. $10.00 SINGLE NUMBER 17/6

EDITORIAL COMMITTEE

THOMAS BEDFORD
SIR ROY CAMERON
C. M. FLETCHER
M. W. GOLDBLATT
ALASTAIR HERON
A. BRADFORD HILL
T. G. FAULKNER HUDSON
R. E. LANE
J. F. LOUTIT
H. B. MAITLAND
A. MEIKLEJOHN
J. N. MORRIS
R. S. F. SCHILLING
J. A. SMILEY
J. R. SQUIRE
EDITOR, *British Medical Journal*

GENERAL ADVISORY BOARD

A. J. AMOR
SIR FREDERICK BARTLETT
SIR HENRY BASHFORD
G. P. CROWDEN
DONALD HUNTER
SIR WILSON JAMESON
T. A. LLOYD-DAVIES
J. M. MACKINTOSH
E. R. A. MEREWETHER
D. C. NORRIS
H. OSMOND-CLARKE
K. M. A. PERRY
DONALD STEWART
SIR REGINALD WATSON-JONES

President of the Association of Industrial Medical Officers and Hon. Editor of the Transactions of the Association of Industrial Medical Officers, *ex officio*

NOTICE TO CONTRIBUTORS

The *British Journal of Industrial Medicine* is intended for the publication of original contributions in industrial medicine from workers of any nationality. It also provides a section for book reviews.

All papers submitted for publication should be referred to The Editor, British Journal of Industrial Medicine, Griffith House, 280 Marylebone Road, London, N.W.1.

Papers are accepted on the understanding that they are contributed solely to this Journal, and that they are subject to editorial revision. Papers should be prefaced by an abstract of the argument and findings and should be more comprehensive than a summary, which will not be required. Papers must be typewritten on one side of the paper only, in double spacing, and with a margin of at least 1¼ in. Photographs and photomicrographs should be printed on glossy paper, and should be unmarked. Charts and graphs accompanying papers should be carefully drawn in black ink on tracing linen or Bristol board or stout, smooth, white paper. Any lettering on these drawings to be done in the editorial office should be lightly inserted in pencil.

References should be arranged according to the Harvard system. When a book is referred to, the place and year of publication, edition, and page should be given. In the text the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (a, b, c) after the date. No numbering of references is necessary.

Contributors will receive one proof, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of 10s. per sheet of 16 pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Twenty-five free reprints of articles will, if desired, be given to contributors. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of costs will be given on application to the Publishing Manager, British Medical Association.

Papers which have been published become the property of the *British Journal of Industrial Medicine* and permission to republish must be obtained from the Editor.

Application for advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

NOTICE TO SUBSCRIBERS

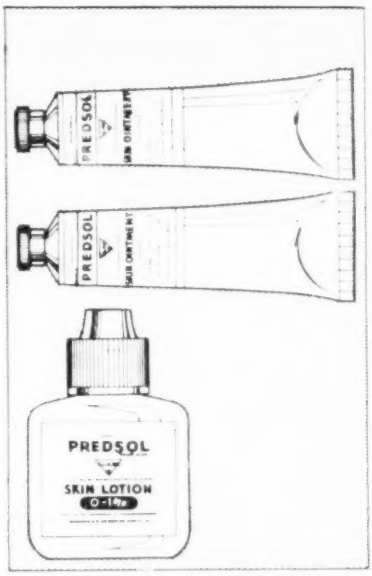
Subscriptions are payable to the British Medical Association. Address: British Medical Association House, Tavistock Square, London, W.C.1.

For the most efficient

treatment of dermatitis,

wet or dry,

infected or not,



PREDSOL

PREPARATIONS

formulated for

each individual case

No one corticoid preparation is likely to suit all inflammatory skin disorders or all stages of a particular case. Glaxo thus present PREDSOL, the water-soluble prednisolone, in a range of preparations to suit every need. Cosmetically they are the most acceptable, therapeutically the most efficient, corticoid preparations for topical application.

(PREDSOL is a Glaxo trade mark)

QUICK REFERENCE GUIDE			
	WET or DRY Surfaces	WET (or hairy) Surfaces	DRY Surfaces
NON-INFECTED cases	PREDSOL LOTION Water-miscible base Strengths of 0·1% and 0·25% in bottles of 20 ml	PREDSOL OINTMENT No. 1 (non-greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams	PREDSOL OINTMENT No. 2 (greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams
INFECTED cases	PREDSOL-N LOTION Water-miscible base Strengths of 0·1% and 0·25% in bottles of 20 ml	PREDSOL-N OINTMENT No. 1 (non-greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams	PREDSOL-N OINTMENT No. 2 (greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams
Predsol-N contains 0·5% neomycin sulphate			

A *STRENGTH* FOR EVERY PURPOSE — A *BASE* FOR EVERY SURFACE

PREDSOL prednisolone 21-disodium phosphate (the water-soluble prednisolone)

PREDSOL-N prednisolone 21-disodium phosphate (the water-soluble prednisolone) + neomycin sulphate

Subsidiary companies or Agents in most countries

GLAXO

GLAXO LABORATORIES (1960) LIMITED GREENFORD MIDDLESEX

BYRON 1414

EDITORIAL COMMITTEE

THOMAS BEDFORD	J. F. LOUTIT
SIR ROY CAMERON	H. B. MAITLAND
C. M. FLETCHER	A. MEIKLEJOHN
M. W. GOLDBLATT	J. N. MORRIS
ALASTAIR HERON	R. S. F. SCHILLING
A. BRADFORD HILL	J. A. SMILEY
T. G. FAULKNER HUDSON	J. R. SQUIRE
R. E. LANE	EDITOR, *British Medical Journal*

GENERAL ADVISORY BOARD

A. J. AMOR	J. M. MACKINTOSH
SIR FREDERICK BARTLETT	E. R. A. MEREWETHER
SIR HENRY BASHFORD	D. C. NORRIS
G. P. CROWDEN	H. OSMOND-CLARKE
DONALD HUNTER	K. M. A. PERRY
SIR WILSON JAMESON	DONALD STEWART
T. A. LLOYD-DAVIES	SIR REGINALD WATSON-JONES

President of the Association of Industrial Medical Officers and Hon. Editor of the Transactions of the Association of Industrial Medical Officers, *ex officio*

NOTICE TO CONTRIBUTORS

The *British Journal of Industrial Medicine* is intended for the publication of original contributions in industrial medicine from workers of any nationality. It also provides a section for book reviews.

All papers submitted for publication should be referred to The Editor, British Journal of Industrial Medicine, Griffith House, 280 Marylebone Road, London, N.W.1.

Papers are accepted on the understanding that they are contributed solely to this Journal, and that they are subject to editorial revision. Papers should be prefaced by an abstract of the argument and findings and should be more comprehensive than a summary, which will not be required. Papers must be typewritten on one side of the paper only, in double spacing, and with a margin of at least 1½ in. Photographs and photomicrographs should be printed on glossy paper, and should be unmarked. Charts and graphs accompanying papers should be carefully drawn in black ink on tracing linen or Bristol board or stout, smooth, white paper. Any lettering on these drawings to be done in the editorial office should be lightly inserted in pencil.

References should be arranged according to the Harvard system. When a book is referred to, the place and year of publication, edition, and page should be given. In the text the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (a, b, c) after the date. No numbering of references is necessary.

Contributors will receive one proof, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of 10s. per sheet of 16 pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Twenty-five free reprints of articles will, if desired, be given to contributors. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of costs will be given on application to the Publishing Manager, British Medical Association.

Papers which have been published become the property of the *British Journal of Industrial Medicine* and permission to republish must be obtained from the Editor.

Application for advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

NOTICE TO SUBSCRIBERS

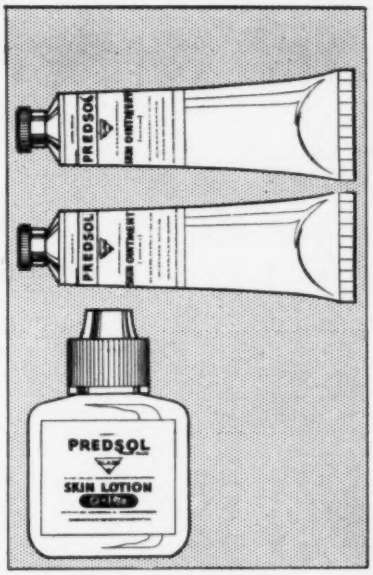
Subscriptions are payable to the British Medical Association. Address: British Medical Association House, Tavistock Square, London, W.C.1.

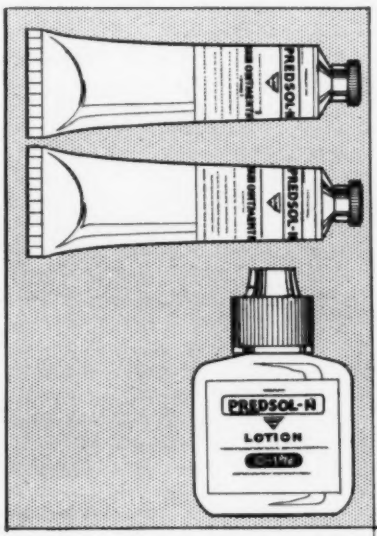
For the most efficient

treatment of dermatitis,

wet or dry,

infected or not,





PREDSOL

PREPARATIONS

formulated for

each individual case

No one corticoid preparation is likely to suit all inflammatory skin disorders or all stages of a particular case. Glaxo thus present PREDSOL, the water-soluble prednisolone, in a range of preparations to suit every need. Cosmetically they are the most acceptable, therapeutically the most efficient, corticoid preparations for topical application.

PREDSOL is a Glaxo trade mark

QUICK REFERENCE GUIDE			
	WET or DRY Surfaces	**WET (or hairy)** Surfaces	**DRY** Surfaces
NON-INFECTED cases	PREDSOL LOTION Water-miscible base Strengths of 0·1% and 0·25% in bottles of 20 ml	PREDSOL OINTMENT No. 1 (non-greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams	PREDSOL OINTMENT No. 2 (greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams
INFECTED cases	PREDSOL-N LOTION Water-miscible base Strengths of 0·1% and 0·25% in bottles of 20 ml	PREDSOL-N OINTMENT No. 1 (non-greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams	PREDSOL-N OINTMENT No. 2 (greasy) Strengths of 0·25% and 0·5% in tubes of 5 and 15 grams
Predsol-N contains 0·5% neomycin sulphate			

A *STRENGTH* FOR EVERY PURPOSE – A *BASE* FOR EVERY SURFACE

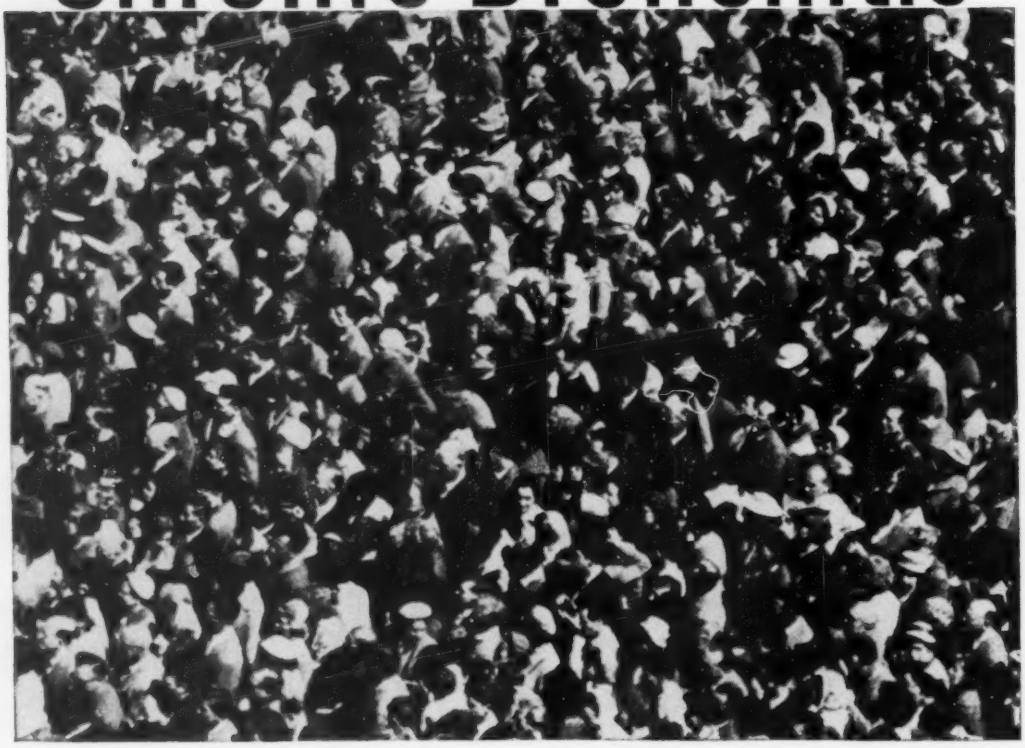
PREDSOL = prednisolone 21-disodium phosphate (the water-soluble prednisolone)

PREDSOL-N = prednisolone 21-disodium phosphate (the water-soluble prednisolone) + neomycin sulphate

Subsidiary companies or Agents in most countries

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX
BYRon 3434

Chronic Bronchitis



The country's greatest problem in respiratory disease

Over £60,000,000 a year in lost productivity and sickness benefit and

Nearly 27,000,000 working days lost through bronchitis each year among the insured

Mounting toll on doctors' time, and hospital beds

Serious increase in number of fatal cases

Calls for the dramatic action of

ACHROMYCIN*

TETRACYCLINE

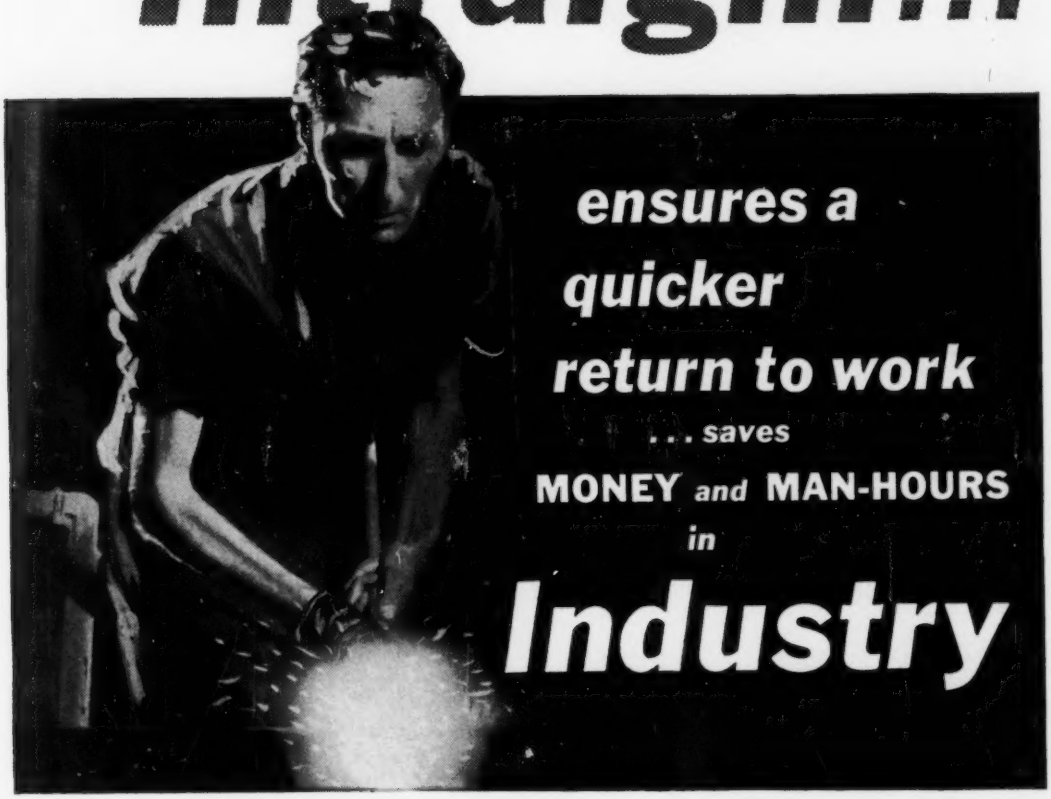
*REGD. TRADEMARK

Lederle LEDERLE LABORATORIES
a division of
CYANAMID OF GREAT BRITAIN LTD. London W.C.2

CYANAMID

In MUSCLE INJURY

Intralgin...



to apply **Intralgin Liquid**
(8 & 32 oz. bottles ... 6/8 & 19/8 plus P.T.)

bandage a wet dressing in position

... to apply **Intralgin Gel**
(50 gramme tube ... 3/4 plus P.T.)
use liberal amount and gently rub in
... for a more intense effect
—warm area first

Samples and literature are available on request

Intralgin applied externally rapidly relieves muscular pain

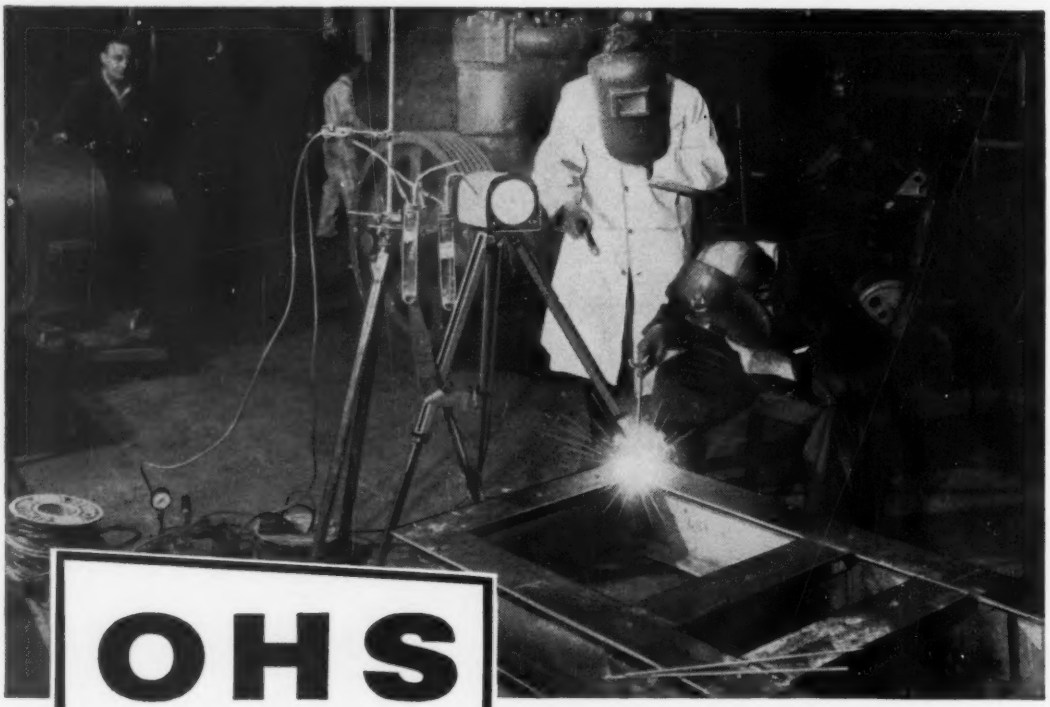
Intralgin combines BENZOCAINE and SALICYLAMIDE which penetrate the skin and act locally in muscles to relieve pain resulting from SPRAINS ... STRAINS ... and INJURIES —by crush or impact.

RIKER

'Intralgin' is a registered trade mark of

RIKER LABORATORIES LIMITED LOUGHBOROUGH LEICESTERSHIRE

11/59-In 1



OHS

The illustration shows air-sampling for fumes and gases evolved during welding. These samples will be analysed in the Laboratories; the results will assist in determining whether a hazard to health exists.

This Consulting and Laboratory Service is now extended to Industry and Commerce throughout the country. Problems of Health and Comfort are investigated and advice given on means of correcting undesirable conditions.

Investigations are carried out under the following headings:

ENVIRONMENTAL
- Lighting surveys
- Heating and ventilation studies
- Noise measurements and analyses

AIR CONTAMINATION
- Dust counts and particle size analyses
- Dust analyses
- Toxic gas, vapour and fume determinations

CLINICAL—to include:
- Blood studies
- Urine analyses
- Audiometry
- X-ray examinations

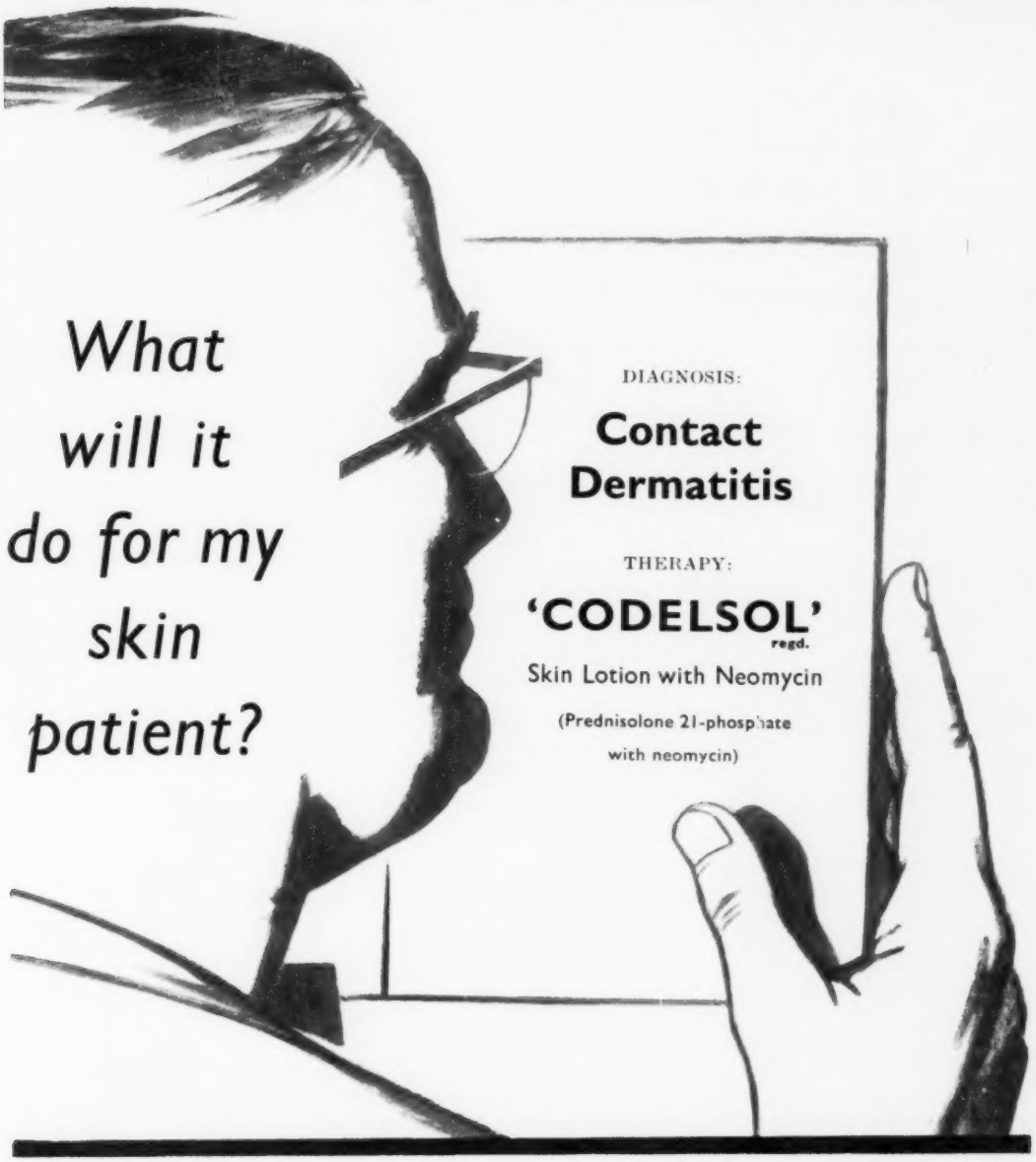
OHS *OCCUPATIONAL HYGIENE SERVICE*

Prospectus from the Secretary—B

OCCUPATIONAL HYGIENE SERVICE

Slough Industrial Health Service, Farnham Road, Slough

Telephone: Slough 22238



Q. Can 'Codelsol' Skin Lotion be used in the presence of infection?

A. 'Codelsol' Skin Lotion contains neomycin which is both safe and highly effective in the treatment of skin infections.

Q. Is 'Codelsol' Skin Lotion easy to apply?

A. Yes. It possesses unique spreading properties, even over hairy surfaces, and this permits better penetration of the affected parts.

Q. For what other conditions is 'Codelsol' Skin Lotion indicated?

A. The vast majority of allergic and inflammatory skin lesions, particularly where large areas are involved.

Q. How does 'Codelsol' Skin Lotion differ from other steroid lotions?

A. It is not a suspension but a fully-soluble solution of prednisolone in a highly effective form.

How supplied: 'CODELSOL' Skin Lotion with Neomycin is available in 15 ml. plastic squeeze bottles. Each ml. contains 5.0 mg. of prednisolone 21-phosphate and 5.0 mg. of neomycin sulphate. The United Kingdom basic N.H.S. cost is 16/0d. per 15 ml.

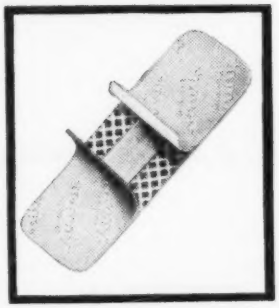
MERCK SHARP & DOHME LIMITED · HODDESDON · HERTS MSD

Elastoplast Airstrip

TRADE MARK

FIRST-AID DRESSING

Any place such as a hospital or factory where a large number of people are leading active lives has a fairly high incidence of minor wounds over a period of time.* Elastoplast 'Airstrip' is made from a specially developed plastic material, through which sweat and skin exudates evaporate at the same rate as they develop on the skin. The material is a micro-porous extensible filter, and is not perforated. It provides a barrier to water, grease and infective organisms.



*". . . *nearly 500,000 skin injuries occur each day which require at least a first-aid dressing.*" *Brit. med. J.* 1956, **2**, 962.
Published work: Trans. Ass. industr. med. Off. IV, 69; Brit. med. J., 1956, **2**, 962; J. Pharm. Pharmacol., 1957, **9**, 785—801; ibid, 1957, **9**, 802—809.

S&N SMITH & NEPHEW LIMITED, WELWYN GARDEN CITY, HERTS.

PERNOMOL
Regd. TRADE MARK

CHILBLAIN PAINT

Colourless *Easily Applied*
Quick drying *Non-staining*

Soothes instantly, encourages rapid reduction of inflammation and promotes healing.
Pernomol can be applied to broken chilblains, but early treatment will prevent this complication.
Pernomol is applied directly and economically from the convenient pocket vial (in aluminium case).
Pernomol is free from sensitization. It is not advertised to the public and can be prescribed on N.H.S. Form E.C.10.

N.H.S price per pencil (complete in aluminium case) 2/-.

Active Constituents:

Chlorbutol B.P.	**2 G.**
Phenol B.P.	**0·95 G.**
Camphor B.P.	**10 G.**
Tannic Acid B.P.	**2·2 G.**
Sp. Sap. Meth, B.P.	**34 ml.**

Adjusted Formula
for

CERUMOL
Regd. TRADE MARK

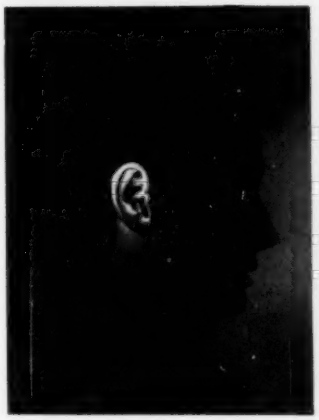
for the easy removal of ear wax

Since some sensitive individuals occasionally complain of a mild smarting in the ear when Cerumol is used, a slight adjustment has been made to the formula and base.

The efficacy of the product is unchanged but the possibility of producing any unpleasant sensation has been eliminated.

Pack for surgery use:- 10 ml. Vial—separate dropper included—Basic N.H.S. Cost 2/8d.

Pack for hospital use:- 2 oz. bottles.

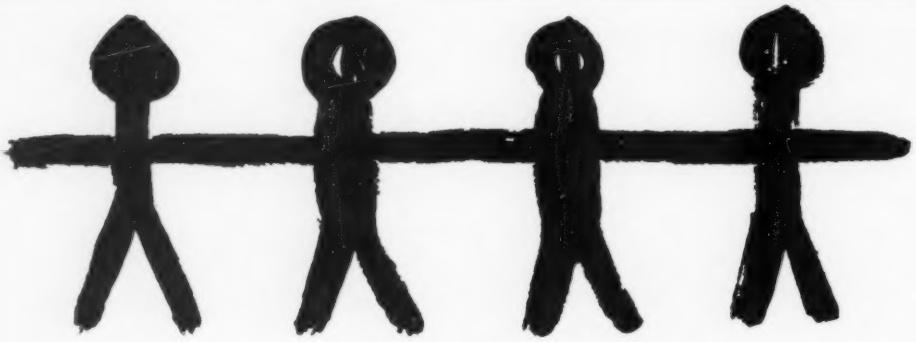


The formula is now as follows:—
Active constituents per 100 *ml.*

p-dichlorobenzene B.P.	**2 G.**
Benzocaine B.P.	**2·7 G.**
Chlorbutol B.P.	**5·0 G.**
Ol. Terebinth B.P.	**10 ml.**

If you would like to test this slightly adjusted formula please write or telephone us for a sample.

LABORATORIES FOR APPLIED BIOLOGY LTD.
91 AMHURST PARK, LONDON, N.16 TELEPHONE: STAmford Hill 2252/3



10 unknown diabetics in every GP's care...

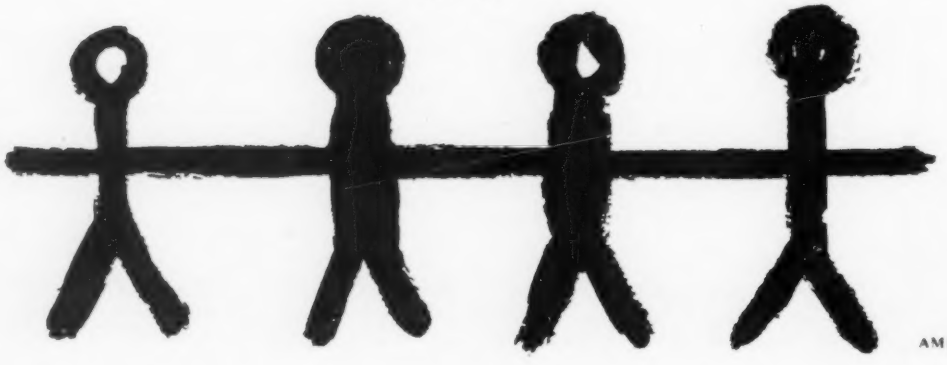
The diabetic population of Great Britain numbers almost 500,000 — yet only about half of them are known and under treatment. Statistically this means that every general practitioner has more than ten undetected diabetics in his care.
These unknown diabetics are at risk. Many already show retinal changes and other vascular abnormalities at the time of diagnosis. These changes are often irreversible: their prognosis could only be improved by early diagnosis and treatment of diabetes.
CLINISTIX* is the best aid to the diagnosis of diabetes. This simple dip-and-read test is specific for glucose: it takes only a few seconds, and has the correct sensitivity for significant results. Every patient whose urine is positive to CLINISTIX should be regarded as a potential diabetic.

to detect diabetes simply dip-and-read Clinistix

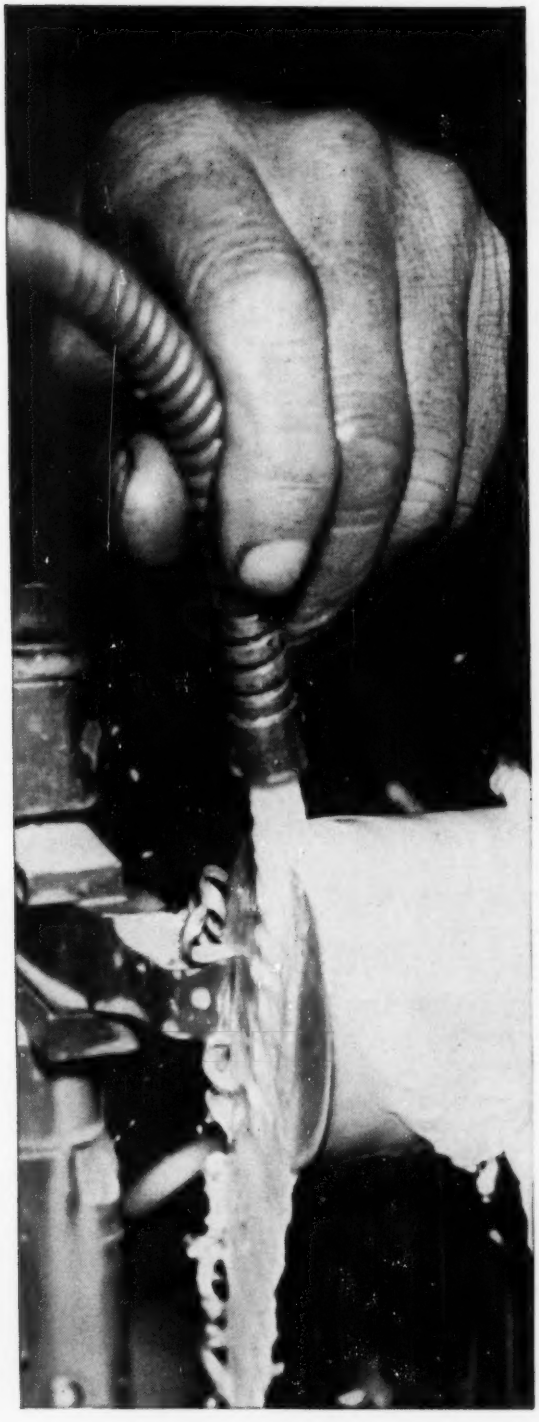
CLINISTIX Reagent Strips are available in bottles of 60 strips.
U.K. Retail Price 6/-, less professional discount. From all chemists.

Ames Company
Nuffield House Piccadilly London W 1

*Trade Mark



AM142



TRIUMPHS OF SHELL RESEARCH

More safety for hands— less worry for you with New Shell Dromus Oils

Shell have produced a new range of soluble cutting oils which will lessen one problem for Works Medical Officers. These new oils reduce the chance of skin troubles for machine operators, caused by the use of phenolic compounds as coupling agents in modern soluble cutting oils.

The phenolic compounds have been used to promote better blending and easier mixing, and the problem facing Shell research chemists was to find the best alternative. They found one which has a higher fatty alcohol complex and they have thus been able to reformulate the Shell range of Dromus Oils.

The New Dromus Oils are every bit as efficient as before and cost no more. They put management in the position of being able to reduce working hazards at no extra cost.

Full information will gladly be supplied about these new oils. And a trial for any industrial medical officer can be arranged. Write to the Lubricants Department, Shell-Mex and B.P. Ltd., Shell-Mex House, London, W.C.2.

NEW SHELL DROMUS SOLUBLE CUTTING OILS

another proof of Shell leadership in lubrication

FOR

SUB-ACUTE and Chronic dermatoses

TAR + HYDROCORTISONE

combined in

TARCORTIN
CREAM

have pronounced advantages over either medicament alone

The established germicidal, stimulating and anti-pruritic properties of tar, in the treatment of sub-acute and refractory skin affections, can now be considerably enhanced by its incorporation with hydrocortisone. *Clinical trials have shown that the two medicaments together exert a powerful synergistic action that is far more rapid, more pronounced and complete than the action of either alone. These two valuable therapeutic agents are presented in a non-greasy, stainless, hydrophilic cream, known as TARCORTIN.

TARCORTIN CREAM
is supplied in 7 grm. and 15 grm. tubes,
containing 0.5% Hydrocortisone in
a special coal-tar extract.
***Literature available**
on request.

STAFFORD-MILLER LIMITED · HATFIELD · HERTS
Manufacturing Chemists
By arrangement with Reed & Carnrick, Jersey City, U.S.A. (Est. 1860)

save systemic antibiotics for systemic uses in skin and eye infections use the potent antibiotic specifically for local use

Framygen

Framycort

Framygen and Framycort preparations all contain Framycetin—the potent antibiotic that is specifically for local use. Framycetin is bactericidal, and it is effective against all the pathogens commonly found in skin and eye infections. Bacterial resistance is very rare, and patient sensitivity has not been reported.

Framycetin on the skin

FRAMYGEN CREAM Framycetin sulphate 0.5%.

FRAMYCORT LOTION Framycetin sulphate 0.5%, hydrocortisone acetate BP 0.5%.

FRAMYCORT OINTMENT As the lotion, but in a greasy ointment base.

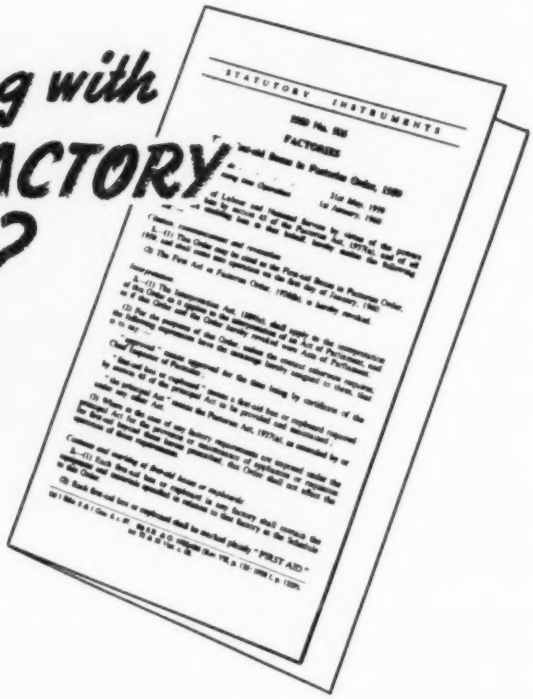
Framycetin on the eye

FRAMYGEN OPHTHALMIC OINTMENT Framycetin sulphate 0.5%.

FRAMYCORT OPHTHALMIC OINTMENT Framycetin sulphate 0.5%, hydrocortisone acetate BP 0.5%.

Genatosan Ltd Loughborough Leicestershire GS38

Are you complying with these REVISED FACTORY REGULATIONS?



Revised regulations regarding First Aid in Factories are effective from 1st January, 1960.

As the Pioneers of Industrial First Aid, we offer approved complete First Aid Outfits to meet the requirements of all trades.

Please state number of employees and nature of business when ordering.

Full details are available to responsible officials applying on their company's letterhead, mentioning this "British Journal of Industrial Medicine" announcement.

CUXSON, GERRARD & Co. Ltd.

OLDBURY · BIRMINGHAM

TELEPHONE: Broadwell 1355

Brit. J. industr. Med., 1960, **17**, 1.

A CLINICAL AND ENVIRONMENTAL STUDY OF BYSSINOSIS IN THE LANCASHIRE COTTON INDUSTRY

BY

S. A. ROACH and R. S. F. SCHILLING

From the Occupational Health Unit, the London School of Hygiene and Tropical Medicine

(RECEIVED FOR PUBLICATION DECEMBER 4, 1959)

The prevalence of byssinosis was measured in a population of 189 male and 780 female workers employed in three coarse and two fine cotton mills. Ninety-eight per cent. of the male and 96% of the female population were seen.

The workers were graded by their histories as follows:—

Grade 0—No symptoms of chest tightness or breathlessness on Mondays

Grade ½—Occasional chest tightness on Mondays, or mild symptoms such as irritation of the respiratory tract on Mondays

Grade 1—Chest tightness and/or breathlessness on Mondays only

Grade 2—Chest tightness and/or breathlessness on Mondays and other days

The dust concentrations to which the workers were exposed were measured with a dust-sampling instrument based on the hexhlet. Altogether 505 working places were sampled. In the card-rooms of the coarse mills 63% of the men and 48% of the women had symptoms of byssinosis. In the card-rooms of the fine mills the corresponding prevalences were 7% for the men, and 6% for the women. Prevalences were low in the spinning-rooms in the coarse mills. The mean dust concentrations in the different rooms ranged from 90 mg./100 m.^{3} in one section of the card-room in a fine mill, to 440 mg./100 m.^{3} in one of the card-rooms of the coarse spinning mills. The prevalence of byssinosis in the different rooms was closely related to the overall dustiness ($r = 0{\cdot}93$). For the three main constituents of the dust, namely, cellulose, protein, and ash, the prevalence of byssinosis correlated most highly with protein, particularly with the protein in the medium-sized dust particles, *i.e.*, approximately 7 microns to 2 mm.

The symptoms of byssinosis may be caused by something in the plant débris which affects the respiratory tract above the level of the terminal bronchioles. This is the site where the medium-sized dust deposits. The possible importance of the fine dust is discussed.

For routine measurements in industry, it is necessary to have a method of assessing dustiness in which the sampling equipment is simple and assessment rapid. As total dust concentration is relatively easy to measure, and correlates closely with the prevalence of byssinosis, permissible levels of dustiness have been expressed in terms of total dust. On comparing the prevalence of byssinosis among workers with short and long exposures and low and high concentrations (Table 11), it appears that a mill with a concentration of 100 mg./100 m.^{3} or less would be reasonably safe, but in dusty card-rooms it seems that such levels are not possible to achieve at present. As it is necessary to adopt a realistic target that can be achieved, it is suggested that dust concentrations in cotton mills should be less than 250 mg./100 m.^{3} and that periodic medical examinations should be adopted to protect susceptible workers who can be advised to leave their dusty environment before they are permanently disabled.

For more than a century, byssinosis has been known to occur in Lancashire cotton mills (Kay, 1831). It has also been found in other industries in which vegetable fibres are processed, namely, flax and hemp (Werner, 1955) but apparently not in jute (Schilling, 1956).

In the Lancashire cotton industry, byssinosis is more prevalent in mills spinning coarse cotton than in mills spinning fine cotton; and in the card-rooms the prevalence is highest amongst those working near the carding engines (Schilling, 1956).

Byssinosis is caused by the dust produced when

the cotton is cleaned and prepared for spinning in the mixing, blow, and card-rooms. In the mixing-room, bales of cotton are opened. In the blow-room, dust and short fibres are beaten and blown out of the cotton. In the card-room, the fibres are combed by the carding engine, which process also removes dirt and defective material. The fibres are gathered and twisted into a thin strand or sliver which is drawn out on other machines into a finer strand ready for spinning. The spinning-rooms are less dusty than the other rooms. Nevertheless, some spinning-room workers do have byssinosis although it is usually mild (Schilling, Hughes, Dingwall-Fordyce, and Gilson, 1955). The airborne dust consists of particles ranging in size from fibres up to 1½ in. long down to particles smaller than 0·2 microns in diameter. The dust is a mixture of broken cotton fibres, plant débris, minerals, bacteria, and fungi (Drummond, Hamlin, Donoghue, and Brownsett, 1954). Also the differences in the prevalence of byssinosis suggested that there is more airborne dust in mills spinning coarse than in mills spinning fine cotton. Therefore we decided to measure the prevalence of disease and dust conditions in the card-rooms and adjacent processes of a group of coarse and fine cotton mills.

The main object was to determine safe levels of dustiness in the atmosphere and to give the cotton industry a target for dust prevention. It was hoped that this study might also help to identify the causal agent and to determine the size range of the particles causing the disease.

Methods

Clinical Diagnosis.—In byssinosis there are no specific radiographic or clinical signs (Schilling *et al.*, 1955). The workman notices a tightness of his chest on Mondays or on the first day at work after an absence. If he leaves the industry at this stage, symptoms cease. If he stays, the symptoms persist and chest tightness and breathlessness may extend to other working days until eventually he becomes severely and permanently disabled. The clinical history was used to estimate the prevalence of byssinosis. It has been found that this method of diagnosis is reliable (Schilling, 1956).

The occupational history was recorded and detailed questions were asked about complaints of cough, chest tightness, and breathlessness. In the present study the workers were graded by their histories as follows:—

Grade 0—No symptoms of chest tightness or breathlessness on Mondays

Grade ½—Occasional chest tightness on Mondays, or mild symptoms such as irritation of the respiratory tract on Mondays

Grade 1—Chest tightness and/or breathlessness on Mondays only

Grade 2—Chest tightness and/or breathlessness on Mondays and other days.

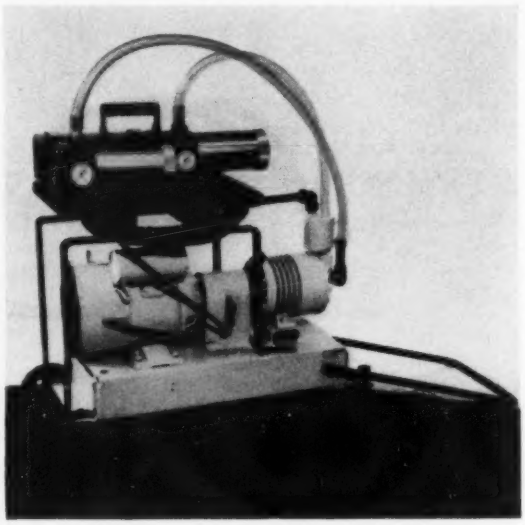


FIG. 1.—The dust sampling machine.

Dr. I. T. T. Higgins, of the Pneumoconiosis Research Unit, and Dr. J. P. W. Hughes, late of the Department of Occupational Health, Manchester University, helped with the clinical survey.

Dust Measurement and Analysis.—It was decided to measure the concentration of airborne dust particles of sizes likely to deposit in the bronchi, because the clinical history of byssinosis suggests that the bronchi are affected. It was also decided to separate the long fibres of cotton floating in the air from the rest of the dust during the sampling because they were unlikely to penetrate very far into the respiratory tract. Since it has been assumed that the finest particles which deposit in the alveoli are responsible for byssinosis (Middleton, 1932; Prausnitz, 1936; Ministry of Labour and National Service, 1952; Schilling, 1956), the concentration of this very fine dust was also measured.

The dust was analysed to derive indices of the concentration of the three main parts of the dust, namely, (1) cellulose, from broken cotton fibres and cotton plants; (2) protein, from the pods, seeds, leaves, and twigs of the cotton plant, and (3) minerals, derived mainly from the soil in which the cotton grows.

The apparatus used (Fig. 1) to measure dust concentration is based upon the hexhlet described by Wright (1954). Air is drawn at a constant flow rate through a filter paper. The suction is provided by a vacuum pump driven by an electric motor and the flow rate is controlled with a critical orifice. The filter papers used were low-resistance, high-efficiency Tullis Russell discs, 7 cm. diameter, weighing about 0·3 g. The flow rate used was 100 l./m. and each run lasted a shift (eight to nine hours). The filter paper is dried and weighed before and after each sample is taken. The difference in weight gives the weight of dust collected.

A hexhlet normally has a horizontal elutriator at the inlet end. Each apparatus had two hexhlets running in

parallel, in one of which the horizontal elutriator is removed and replaced by a 7 cm. diameter wire gauze with square holes 2 mm. × 2 mm. In the hexhlet with the elutriator, only fine dust is collected.

The size, density, and shape of dust particles determines their dynamic behaviour when suspended in air and how deep into the lung they penetrate before depositing. These properties also determine their speed of settling under gravity in a similar way.

The elutriator of a hexhlet is designed to separate the coarse particles from the air passing through it so that only the fine particles which would reach the alveoli and terminal bronchioles collect on the filter paper.

The elutriator consists of a bank of parallel plates of which the total floor area is such that 50% of the particles with an equivalent diameter of 5 microns deposit on the plates and 50% pass on. The "equivalent" diameter of a particle is equal to the diameter of a unit density sphere of which the falling velocity is equal to that of the particle. Most of the particles smaller than 5 microns pass through the elutriator and most larger particles deposit on the plates. The proportion of particles passing the elutriator decreases with increasing equivalent diameter. Particles larger than 7·1 microns equivalent diameter do not pass through (see Fig. 2). The dust deposited on the plates is rejected.

In the hexhlet with the wire gauze replacing the elutriator, the dust collected consists of particles with dimensions up to 2 mm. Long fibres collect on the outside of the gauze. These are wiped off periodically during each run and subsequently weighed and analysed. This dust we call "coarse" dust. The dust which penetrates the gauze we call "medium and fine" dust and the dust which penetrates the elutriator we call "fine" dust. Thus the amount of "medium" dust is obtained by difference.

The filter papers with dust on them were cut in half and one half was used to estimate the amount of protein and the other half to estimate the amount of mineral. The remainder was assumed to consist mostly of cellulose from the cotton fibres and plant débris. The protein was estimated by determining the amount of organic nitrogenous material with a micro-Kjeldahl apparatus.

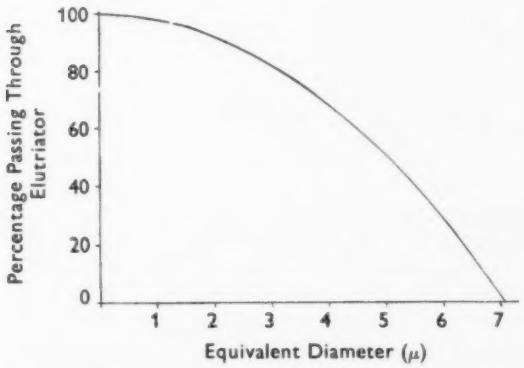


FIG. 2.—Curve denoting the proportion of particles of different sizes passing through the horizontal elutriator of a hexhlet.

The mineral content was estimated by ashing the sample and weighing the ash. Most of the samples were weighed and analysed in the chemistry department of the Pneumoconiosis Research Unit under Dr. T. G. Morris. This analysis of the dust into three components is essentially the same as that described by Silverman and Viles (1950).

Mills Studied

Two groups of mills in Lancashire were included in this study. Their conditions had not changed substantially for 25 years and they were believed to be dusty. In one there were three mills, spinning low-grade coarse cotton from the U.S.A. and Nigeria, and in the other there were two mills, spinning high-grade fine cotton from Sea Island and the Sudan.

Populations.—The clinical studies of the workers in the card, blow, and mixing-rooms were made in the summer and autumn of 1955. The spinning-room operatives of the coarse mills were examined in the autumn of 1956.

The population studied was all those working in these rooms at the start of the survey. Those under the age of 25 working in the spinning-rooms were not examined. Ninety-eight per cent. of the men and 96% of the women in the defined population were seen. No one refused (Table 1).

TABLE 1
POPULATIONS IN THE MILLS

	Coarse Mills		Fine Mills	Total
	Card-Blow- and Mixing-room Workers	Spinning-room Workers	Card-Blow- and Mixing-room Workers	
Men				
Seen and graded	73	50	62	195 (98%)
Away sick	—	1	1	2
Left during survey	2	—	—	2
Total	75	51	63	189
Women				
Seen and graded	231	355	163	749 (96%)
Away sick	1	8	4	13
Left during survey	11	2	5	18
Total	243	365	172	780

Airborne Dust.—The dust samples were taken between 1955 and 1957. To measure the dust exposure of the workers a list of names of those in each room was first obtained. These names were placed in random order and samples were taken successively alongside these workers until about 50 working places in each main

TABLE 2
PLACES SAMPLED FOR DUST

	Coarse Mills		Fine Mills	Total
	Card-Blow- and Mixing-rooms	Spinning-rooms	Card-rooms	
No. of working places sampled	205	191	109	505

room had been covered (see Oldham and Roach, 1952). Each sample lasted a shift and the instrument was left at the working place all day. It was put as near to the worker as possible without interfering with his work. Normally, three samples were obtained each day: a sample of fine dust, of fine and medium dust together, and of coarse dust. Samples were taken at 505 working places (Table 2).

The sampling machines were attended by mill overlookers who were given detailed instructions about where and when to take the samples. Checks were made from time to time to ensure that this was done correctly.

Results

Prevalence of Byssinosis.—In the coarse mills, the prevalence of byssinosis was high in the card-room workers (51%) and low in the spinners (2%) (Table 3). In the mixing- and blow-room workers, of whom there were 27, 11 (41%) had byssinosis.

In the fine mills the prevalence of byssinosis was low in the card-room workers (6%) and none of the eight mixing- and blow-room workers had byssinosis.

Within the card-rooms, the nearer workers were to the carding engines the higher was the prevalence of disease (Table 4).

Schilling (1956) found similar trends in a survey of card-room workers in coarse and fine mills.

Dust Concentrations.—There was a wide range of dust concentrations in all the workrooms; but generally the concentrations were higher in the coarse than in the fine mills and higher near the carding engines than in other positions in the card-room (Table 5).

Monday Symptoms and Dust Concentrations.—In Table 6 we give a summary of the dust sampling results in card-rooms on different days of the week. The mean concentration of dust was lower on Mondays than on other days. Drummond *et al.* (1954) also found that the concentration of airborne

TABLE 3

PREVALENCE OF BYSSINOSIS

	Coarse Mills										Fine Mills				
	Card-rooms					Spinning rooms					Card-rooms				
	No. of Workers	No. with Byssinosis			Total	No. of Workers	No. with Byssinosis			Total	No. of Workers	No. with Byssinosis			Total
		Grades					Grades					Grades			
		½	1	2			½	1	2			½	1	2	
Men	52	4	19	10	33 (63%)	50	2	3	0	5 (11%)	56	1	2	1	4 (7%)
Women	225	25	65	19	109 (48%)	355	2	2	0	4 (1%)	161	3	4	2	9 (6%)

TABLE 4

PREVALENCE OF BYSSINOSIS IN CARD- AND SPINNING-ROOMS

Place of Work*	Coarse Mills		Fine Mills	
	No. of Workers	No. with Byssinosis	No. of Workers	No. with Byssinosis
At or near carding engines	123	77 (63%)	32	7 (22%)
Elsewhere in card-room	96	43 (45%)	175	6 (3%)
Spinning-rooms	405	9 (2%)	—	—

*Those who worked in more than one place have been excluded from this table.

TABLE 6

MEAN CONCENTRATION OF DUST IN CARD-ROOMS ON DIFFERENT DAYS OF THE WEEK

Day of Week	Total Dust (Mean Concentration mg. per 100 m.³)	No. of Samples*
Monday	331	34
Tuesday	360	36
Wednesday	368	32
Thursday	397	37
Friday	360	32

*Including all total dust samples obtained in card-rooms of coarse mills and around carding engines in fine mills.

TABLE 5

AIRBORNE DUST CONCENTRATIONS IN CARD- AND SPINNING-ROOMS

Sampling Position	Total Dust Concentration in mg./100 m.³					
	Coarse Mills			Fine Mills		
	Workplaces Sampled	Mean Concentration	Range	Workplaces Sampled	Mean Concentration	Range
At or near carding engines	105	440	110-1370	36	320	60-660
Elsewhere in card-room	57	330	80-810	73	90	50-210
Spinning-rooms	191	150	30-350	Not measured		—

dust on Mondays was no higher than on other days. Thus, it appears that the characteristic Monday symptoms of byssinosis are not due to higher dust exposures on this day.

Size Distribution and Chemical Analysis of the Dust.—The size distribution of the dust is summarized in Table 7.

TABLE 7
SIZE DISTRIBUTION OF THE DUST

Type of Mill	Room	Percentage by Weight in Size Range		
		*Fine (< than 7 microns)	*Medium (7 microns to 2 mm.)	*Coarse (> than 2 mm.)
Coarse	Card	7	30	63
	Spinning	6	10	84
Fine	Card	5	34	60

*See section on dust measurement and analysis for detailed definition.

In all the rooms, less than 8% by weight of the dust consisted of fine particles. The coarse dust, which collects on the outside of the gauze, accounted for 60% or more of the dust.

A summary of the chemical analysis of the dust is given in Table 8. In all rooms the coarse dust contained 85% or more cellulose. This was expected, since it is mainly cotton fibres. On the other hand, the medium and fine dust had much higher proportions of protein and minerals.

TABLE 8
CHEMICAL ANALYSIS OF DUST

Type of Mill	Room	Size of Dust	Proportion by Weight (%)		
			Cellulose	Protein	Minerals
Coarse	Card	Fine	45	21	34
		Medium	51	21	28
		Coarse	85	8	7
	Spinning	Fine	27	27	47
		Medium	50	14	36
		Coarse	94	3	3
Fine	Card	Fine	36	21	43
		Medium	53	15	32
		Coarse	86	7	7

TABLE 9
PREVALENCE OF BYSSINOSIS IN 10 GROUPS OF WORKROOMS

Type of Mill	Mill No.	Workroom(s)	No. of Workers	No. with Byssinosis
Coarse	1	Top card-room	14	1 (7%)
Coarse	1	Bottom card-room	20	4 (20%)
Coarse	2	Both card-rooms	19	17 (89%)
Coarse	3	Both card-rooms	42	23 (55%)
Fine	4 & 5	Card-rooms	9	2 (22%)
Fine	4 & 5	Combing-rooms	70	2 (3%)
Fine	4 & 5	Frame-rooms	43	1 (2%)
Coarse	1	Both spinning-rooms	15	0
Coarse	2	Both spinning-rooms	27	1 (4%)
Coarse	3	Both spinning-rooms	50	0
		Total	309	51 (17%)

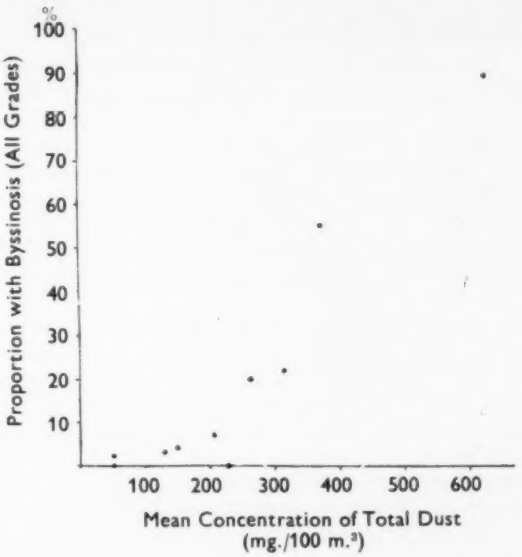


FIG. 3.—Airborne concentration of dust related to prevalence of byssinosis.

Byssinosis and Dust Concentration.—The relationship between prevalence of byssinosis and dust concentration was examined in 10 groups of workers who had spent 95% or more of their time in one room or pair of similar rooms. The prevalence in these groups is given in Table 9.

The degree of association between the dust concentration and prevalence of byssinosis in these 10 groups can be expressed as a correlation coefficient. The correlation of the concentration of total dust with the prevalence of byssinosis was 0·93 (Fig. 3). The relative importance of different fractions of the dust can be examined by comparing the extent to which their concentrations are correlated with prevalence.

The cotton fibres, which consist mainly of cellulose, are unlikely to be responsible for byssinosis since cellulose is a very stable substance and insoluble in water or other common solvents. However, it may be contributory as a mechanical irritant.

The minerals in the dust, being derived principally from the soil, will consist mainly of silicates and silica. The airborne concentration of the "ash" fraction of the dust lies between 10 mg./100 m.³ and 80 mg./100 m.³ In industries where a risk of pneumoconiosis due to mineral dust is present the concentration of dust is usually some 100 times greater than that in these cotton mills. Therefore, it is not likely to be important in byssinosis. This is confirmed by the absence of specific radiological changes in cotton workers. However there may

be some chemical in the mineral fraction which is contributory at least in part to byssinosis.

The third fraction of the dust, the brittle and dried plant débris other than cotton fibres, is found only in the cotton industry and other industries processing vegetable fibres and will consist of a variety of complex organic compounds, mainly proteins and carbohydrates many of which are easily soluble in water. Of the three major constituents this plant débris would seem by exclusion to be the one most likely to contain or be closely associated with the active constituent.

The correlation of prevalence with the airborne concentration of protein was 0·94, with cellulose 0·81 and ash 0·58 (Table 10). The correlation of any one of these with prevalence may be due to the particular constituent being responsible for byssinosis, but may also be due to the constituent being closely correlated with one of the other two, which is in turn the responsible agent or closely associated with it. We can compare the degree of association of prevalence with the three constituents and eliminate the effect of any cross correlation by calculating the partial correlations. By this process we estimate the correlation which would have been obtained if the other variables had been constant.

TABLE 10

CORRELATION OF PREVALENCE OF BYSSINOSIS WITH DUST CONCENTRATION

Concentration of	Correlation with Prevalence	
	Total Correlation	Partial Correlation
Total dust	0·93	—
All cellulose	0·81	0·58
All protein	0·94	0·90
All ash	0·58	−0·40
Fine protein	0·58	0·03
Medium protein	0·95	0·55
Coarse protein	0·93	0·14

The partial correlation of prevalence with protein when the effects of the cellulose and ash were eliminated was 0·90. With cellulose it was 0·58 when protein and ash were eliminated and with ash it was − 0·40 when protein and cellulose were eliminated. This suggests that the cotton fibres and the minerals are relatively unimportant and that the active agent in the cotton dust is most likely to be closely associated with the protein.

In a similar way we can examine the relative importance of the different size fractions of the protein in producing this close association, by comparing the extent to which they are correlated with prevalence.

The fine fraction of the dust is the size which can penetrate to the terminal bronchioles and alveoli, the medium fraction of the dust is the size which deposits mainly in the trachea, bronchi, and bronchioles, and the coarse fraction is not likely to penetrate past the nose and mouth. The clinical picture of byssinosis suggests that the bronchi and bronchioles are affected. If this is so, then the medium-sized dust is likely to be the most important size range. The fine dust may also be important as much of it deposits before reaching the alveoli and that which does reach the alveoli may produce a reaction there. When collecting the coarse fraction of the dust it is trapped by the wire gauze at the entrance to the sampler. Some of the medium and fine dust is filtered out by this coarse dust before it is picked off, so that the coarse fraction may contain some of the material which if inhaled would normally penetrate into the bronchi, bronchioles, and alveoli. Because of this the recorded concentration of coarse dust may be found to be associated with prevalance.

The total correlation of prevalence with the airborne concentration of fine protein was 0·58, with medium protein 0·95, and with coarse protein was 0·93.

The partial correlation of prevalence with fine protein, after eliminating medium and coarse protein was 0·03, the partial correlation with medium protein was 0·55 after eliminating fine and coarse protein, and with coarse protein was 0·14 after eliminating fine and medium protein.

The statistical significance of these correlation coefficients is difficult to judge since the variates are not distributed normally (see Fig. 3, Table 10). However, the results suggest that the prevalence of byssinosis was more highly associated with the concentration of medium protein than with the concentration of the other constituents and that the total correlation of prevalence with the other constituents may be largely accounted for by their association with this fraction.

It should be emphasized that this does not in any way prove that byssinosis is caused by the protein in the medium-sized dust. The link, if it exists, may be an indirect one. Also, larger errors in estimating the other constituents may have produced the lower correlations. For example, it is certainly more difficult to determine the concentration of fine protein than medium protein due to the much smaller quantities available for analysis and the difficulty of separating the fine dust during collection.

Permissible Levels of Dustiness.—For routine measurements of dust it is necessary to have a method in which the sampling equipment is simple and the assessment of the samples is rapid. As total dust concentration is easy to measure and

TABLE 11

PROPORTION OF WORKERS* WITH BYSSINOSIS GROUPED BY DURATION OF EXPOSURE AND CONCENTRATION OF DUST

(Byssinosis Grades 1 and 2 only)

Duration of Exposure	Concentration of Dust (mg./100 m.³)											
	0 –		100 –		175 –		250 –		375		500 +	
	No. with Byssinosis	No. in Group	No. with Byssinosis	No. in Group	No. with Byssinosis	No. in Group	No. with Byssinosis	No. in Group	No. with Byssinosis	No. in Group	No. with Byssinosis	No. in Group
0 –	0	14	0	59	0	23	1	17	5	14	3	7
5 –	0	17	0	20	2	14	4	11	3	6	4	7
10 –	0	23	1	30	4	29	9	22	10	18	4	8
20 –	0	18	3	27	2	14	2	3	3	4	1	1
30 –	0	9	2	24	3	10	2	6	1	2	0	1
Total	0	81	6	160	11	90	18	59	22	44	12	24

*Excluding those who had worked in coal-mines or who had spent more than 5% of their period of employment in other cotton mills.

correlates closely with prevalence of byssinosis ($r = 0{\cdot}93$), our permissible levels of dustiness are expressed in terms of total dust.*

There were 458 workers whose experience lay in environments where the dust concentration had been measured. Their duration of exposure and corresponding average concentration are summarized in Table 11. This gives the number of workers and how many of them had byssinosis grades 1 and 2. Although all these workers had chest tightness, many of them were not permanently disabled. However, it is likely that continual exposure to conditions causing these symptoms would eventually give rise to permanent disability.

Amongst those exposed to an average concentration of more than 250 mg. per 100 m.³ there was a high proportion (41%) with byssinosis. Even when the period of exposure was very short a substantial number were affected. Clearly, dust control is essential in any room as dusty as this.

Amongst workers exposed to concentrations of between 100 and 250 mg. per 100 m.³, two workers among those with less than 10 years' exposure had byssinosis. Thus, dust control is also desirable where the concentration lies in this range.

None of those workers exposed to a concentration of less than 100 mg. per 100 m.³ had byssinosis grade 1 or 2. One man with a long experience did complain of occasional chest tightness on Mondays, so that although a card-room with a concentration of less than 100 mg. per 100 m.³ would probably be safe, it would be wise to safeguard the particularly sensitive individuals by periodic medical examinations. With higher concentrations, such examinations are essential in order to protect susceptible workers who can be advised to leave their dusty environment before they are permanently disabled.

*The correlation of prevalence with concentration of fine dust was 0·10.

In summary our results suggest the following classification:—

Grade of Dustiness	Concentration Total Dust
A. Safe, with medical supervision of workers	Less than 100 mg./100 m.³
B. Dust control desirable and medical supervision essential	Between 100 and 250 mg./100 m.³
C. Dust control and medical supervision essential	More than 250 mg./100 m.³

Discussion

In byssinosis the clinical symptom of chest tightness on Mondays seems to be a specific response to inhaling the cotton dust and is very unlikely to be caused by mechanical irritation. The relationship between prevalence of byssinosis and the various components of the dust reported in this paper gives further support to this view and points to some constituent of the plant débris as the active agent.

The dust particles of less than 7 microns diameter are apparently less important than the larger particles. The explanation of this may be simply that there is much more dust in the medium and coarse size ranges. In the card-rooms of the coarse mills, in every 100 mg. of dust there was about 6 mg. of medium protein and 1·5 mg. of fine protein. The agent causing byssinosis seems to be associated with this protein and may in fact be part of it. Thus, the amount of the agent in the fine dust is probably considerably less than the corresponding amount in the dust in the medium size range. Furthermore, the sensation of chest tightness may originate in the respiratory tract above the level of the terminal bronchioles, where most of the medium-sized particles will fall. However, it is not possible to rule out the fine dust altogether. It may be affecting the terminal bronchioles or alveoli without necessarily causing the sensation of chest tightness. It is urgently necessary to be sure of the importance or

otherwise of the fine dust since the fine dust is much more difficult to suppress than is the medium or coarse dust.

Bacteria and moulds have relatively high concentrations in the atmosphere of cotton card-rooms and have been considered as possible causes of byssinosis (Drummond and Hamlin, 1952). In addition, Thiry (1941) has suggested that moulds and bacteria are the causes of the diseases in flax workers. The amount of protein in the dust from bacteria and fungi is very small, but recent work by Tuffnell (personal communication) showed a correlation between prevalence of byssinosis and concentrations of viable organisms of the genus Bacillus. However, when he exposed three men with disabling byssinosis to an inert dust carrying *Bacillus pumilus* and *Aspergillus niger*, the most common species of bacteria and fungi found in cotton mills, they had no clinical symptoms and showed no reduction in ventilatory capacity.

Our suggested grading of workrooms according to dustiness was arrived at after consideration of the prevalence in groups exposed to similar concentrations for similar lengths of time We might have deduced permissible levels of dustiness from dose response curves in a similar way to that suggested by Roach (1953). However, we were hesitant to do this because of the possible effects of selection in those groups with the highest prevalence of byssinosis. People with byssinosis are generally aware that the dust affects their breathing and it is likely that they will leave their jobs more readily than those who are not so affected. To this extent the people working in a cotton mill are likely to be a selected population, particularly those groups who work in the dustiest jobs and are in consequence affected most by dust. To deduce permissible levels of dustiness from dose-response relationships we would have had to assume that selection operates in an exactly similar way in all mills or does not operate at all.

The amount of dust in the air of a cotton mill seems to depend on the quality of the cotton processed, the weight of cotton spun per week, and the amount of ventilation in the rooms. The more dirt, trash, and short fibre there is in the cotton the greater is the concentration of airborne dust. Also the higher the throughput of cotton the greater is the concentration of airborne dust. The dustiness is reduced by increasing the amount of general ventilation and by installing localized extraction hoods around the sources of dust. The simplest way of testing the effectiveness of these methods is by measuring the reduction in total dust concentration. However, this may not reflect the reduction in concentration of the active agent very accurately. In such a variable and indefinite situation, dust concentration is bound to be only a rough and ready index of the byssinosis risk. The final test of the efficiency of any dust extractor must be whether or not the workers in the room develop byssinosis.

The Shirley pressure point system, which is a local exhaust ventilation system applied to the dusty points of a carding engine, substantially reduces the dust concentration in card-rooms with beneficial effects on the operatives (McKerrow, McDermott, Gilson, and Schilling, 1958; Ministry of Labour and National Service, 1957). It is planned to make a further study of the effects of installing it in a dusty card-room on airborne dust concentrations and on the clinical symptoms and ventilatory capacities of the workers. Similar tests will also be made in a dusty card-room which has a device for improving its general ventilation by a plenum system. Thus we shall have a good estimate of the value of these devices in preventing byssinosis. Preliminary results indicate that although the Shirley pressure point system and those systems which increase general ventilation each substantially reduce the dust concentrations, they may not at present achieve safe levels in very dusty card-rooms.

At the present time we do not think it would be wise to recommend a target level of dustiness which could not be achieved in practice, for this would be likely to result in little or no action. Our aim would be initially to adopt a realistic target that could be achieved in the immediate future by reasonably practicable measures, namely that dust concentrations in cotton mills should be less than 250 mg. per 100 m.^{3}

We are grateful to many colleagues for their help in making this investigation, especially Dr. I. T. T. Higgins, Dr. J. P. W. Hughes, Miss I. Dingwall-Fordyce, and Dr. T. G. Morris.

We are specially indebted to the management and workers of the cotton mills. They gave their wholehearted cooperation and without their help these surveys could not have been made.

We would also like to thank the following for help in preparing this paper: Dr. J. C. Gilson, Director of the Medical Research Council's Pneumoconiosis Research Unit, Dr. Douglas Hill, Director of the Shirley Institute, and Professor R. E. Lane of Manchester University.

One of us (R.S.F.S.) received a grant from the Medical Research Council to study byssinosis.

References

Drummond, D. G., and Hamlin, M. (1952) *Brit. J. industr. Med.* **9**, 309, 311.

——, ——, Donoghue, J. K., and Brownsett, F. (1954). *Ibid.*, **11**, 151.

Kay, J. P. (1831). *New Engl. med. surg. J.*, **1**, 357.

McKerrow, C. B., McDermott, M., Gilson, J. C., and Schilling, R. S. F. (1958). *Brit. J. industr. Med.*, **15**, 75.

Middleton, E. L. (1932). Home Office Report of the Departmental Committee on Dust in Card Rooms in the Cotton Industry. H.M.S.O., London.
Ministry of Labour and National Service (1952). 2nd Interim Report on Dust in Card Rooms. H.M.S.O., London.
—— (1957). Dust in Card Rooms: 3rd Interim Report of the Joint Advisory Committee of the Cotton Industry. H.M.S.O., London.
Oldham, P. D., and Roach, S. A. (1952). *Brit. J. industr. Med.*, **9**, 112.
Prausnitz, C. (1936). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 212.
Roach, S. A. (1953). *Brit. J. industr. Med.*, **10**, 220.
Schilling, R. S. F. (1956). *Lancet*, **2**, 261.
——, Hughes, J. P. W., Dingwall-Fordyce, I., and Gilson, J. C. (1955). *Brit. J. industr. Med.*, **12**, 217.
Silverman, L., and Viles, F. J. (1950). *Textile Res. J.*, **20**, 109.
Thiry, U. (1941). *Arch. Mal. prof.*, **3**, 129.
Werner, G. C. H. (1955). *Ibid.*, **16**, 27.
Wright, B. M. (1954). *Brit. J. industr. Med.*, **11**, 284.

Brit J. industr. Med., 1960, **17**, 10

A SURVEY OF SMALL FACTORIES*

BY

MARGOT JEFFERYS and C. H. WOOD

From the Department of Public Health, London School of Hygiene and Tropical Medicine

(RECEIVED FOR PUBLICATION APRIL 27, 1959)

This survey was undertaken by a group of doctors, nurses, and lecturers in the Department of Public Health of the London School of Hygiene and Tropical Medicine as part of the teaching programme for the Diploma in Public Health. Fifty small factories in an area of a metropolitan borough were invited to answer questions concerning their industrial processes, their labour force, their premises, their first-aid provision, and the visits they received from officials of local and central government. Forty-eight of these factories responded and observations were made by teams of three recording independently of each other in 45. A variety of industries was represented in these 48 firms, half of which employed less than 10 workers.

The working environment, in respect of sanitary arrangements, cleanliness and tidiness, lighting on stairs and passage ways, was considered to be unsatisfactory in many firms. Some instances of inadequate safeguards of machines were seen. The accident rate was found to be rather less than the computed national rate for manufacturing industry in 1956.

First-aid equipment and workers were also considered to be deficient in a number of instances. In case of accident and for the treatment of minor ailments most firms made use of a local casualty and out-patient department of a general hospital. This service was considered quite adequate.

Many firms had not been visited by the Factory Inspector or his deputy during the previous year. Rather more had received visits from the local authority health inspectors. Many firms expressed confusion about the duties and functions of their various official visitors.

The conclusions drawn from this limited enquiry were that the working conditions in small factories are often unsatisfactory; that in areas such as the one surveyed it is unrealistic to think in terms of development of an industrial health service similar to those operating in Slough and Harlow; and that the greatest impact on environmental conditions might be made by an improved and simplified system of inspection especially adapted to the needs of the small factory.

There is no specific provision in the National Health Service for industrial medical services. Most large undertakings, however, now employ industrial medical officers and nurses who, by dealing promptly and efficiently with injuries and minor sickness and by investigating environmental hazards, can save the firms and their employees much suffering, time, and money.

The small firm has not the resources to employ full-time medical workers of its own. In some areas—notably Slough and Harlow—industrial health services have been organized on a collective basis; but such schemes are still rare and none of them covers the very smallest firms in the older industrial districts (Slough Industrial Health Service, 1957; Taylor, 1958). Over 80% of the factory establishments in Great Britain employ fewer than 25 workers and the majority of these are located in the large cities of Britain in areas developed in the nineteenth century.

What are conditions like in these small firms? What medical services, if any, do they possess or make use of? Is it worth their while to run an industrial health service on a collective basis?

* This paper is based on the report of a study group of which the following were members:

Dr. R. H. Strudwick (Colonial Medical Service, Hong Kong), Dr. D. Sturman (general practitioner, New Zealand), and Dr. R. E. Woolley (R.A.F. Medical Service) (joint chairmen), Dr. A. Bhoomkar (senior house officer, Osmania General Hospital, India), Dr. E. C. Cummings (Government Medical Service, Sierra Leone), Dr. A. L. Ferguson (house physician, Preston, North Shields), Miss N. A. Jones (public health nurse tutor, Rural Health Training School, Malaya), Dr. R. O. M. Jones (R.A.F. Medical Service), Dr. A. B. Marples (research assistant, Florida State Board of Health, U.S.A.), Miss M. A. O'Keiffe (senior health visitor, Health Department, Trinidad), Miss R. Seymour (public health nurse, British Red Cross, Kenya), Dr. H. Shore (Colonial Medical Service, Uganda), Mr. R. Soedarjono (Ministry of Health, Indonesia), Miss J. K. Wenborn (superintendent nursing officer, Breconshire County Council), Mrs. M. Jefferys and Dr. C. H. Wood (staff members), and Miss J. Campbell (Secretary).

These were the questions which we wanted to investigate. We started our survey in December, 1957, and completed the field work before the report by the Factory Inspectorate on industrial health in Halifax had been published (Ministry of Labour, 1958). The field work was done by doctors and nurses, none of whom had had any special training in factory inspection.

Area and Method

Practical considerations dictated the choice of an area to be investigated. Because time was limited and no special funds were available, we had to choose an area within easy reach of the London School of Hygiene and Tropical Medicine containing the minimum number of factory establishments which would make the investigation worthwhile. We chose, therefore, a near-by ward in a metropolitan borough, which we knew contained about 50 factories. It was an area of mixed, small-scale industry and of residential housing, largely developed in the late nineteenth and early twentieth centuries. In these respects we felt that it resembled many industrial areas in other large towns and in other parts of London.

We obtained a list of all the registered factories within the ward from the Medical Officer of Health, and arranged that each should be visited by a team of three, drawn from the study group. Factory owners or managers were notified in advance that we would be calling and would be grateful for their help.

A copy of the questionnaire used is given in Appendix I. Both the content and the layout had been changed after a preliminary trial. Where possible, the questions were of the Yes/No or multiple choice variety with the answers pre-coded and numbered so that all the recorder had to do during the interview was to ring the appropriate symbol. Some questions, such as number 25, which asked for a description of any accidents happening in 1957, required a more detailed answer which was recorded as nearly as possible verbatim.

Broadly speaking, questions 1-14 related to the number and type of employee and the fabric and age of the premises. Questions 15-18 were concerned with hazards involved in the work, and questions 19-31 referred to the medical arrangements and the provisions for dealing with accidents and environmental hazards. Questions 32-37 concerned visits which the firm might have received from various authorities.

For the assessment of the environment, each of the three observers had a separate card and filled it in independently immediately after inspecting the factory. A copy of the card is also given in Appendix I. These assessments were essentially subjective judgments. They were phrased in such a way that the answer "yes" implied an unfavourable assessment. In addition, there was space on the card for the observer's general impression of the factory and for notes on any hazards which he thought were not adequately dealt with by the management or workers. We also drew up a schedule of instructions and definitions to ensure that, amongst ourselves, we achieved as great a degree of uniformity of judgment as possible.

The main enquiry took place during January and February, 1958. Each week, five teams (consisting of different combinations of individuals on each occasion) visited three factories. At each factory the answers to our questions were filled in by one member of the team acting as recorder; every member of the group acted as recorder for at least one interview.

Results

Size and Nature of Sample.—The area selected contained 50 factories. Of these, 48 answered our questions and 45 allowed a visit to their works. The number of employees ranged from 180 in one factory to one man working alone in another. The distribution of factories by size, compared with the national figures, is given in Table 1.

TABLE 1

NUMBER AND PERCENTAGE OF FACTORIES BY NUMBER OF EMPLOYEES IN SURVEY AREA AND IN GREAT BRITAIN

Number of Employees	Survey Area	Great Britain* (%)
1 – 10	23 (48%)	69
11 – 25	16 (33%)	14
26 – 50	3 (6%)	7
51 – 100	5 (10%)	4
101 +	1 (2%)	5
Total	48 (100%)	100 No. = 233,519

* Figures obtained from the report of the Halifax Survey (1958)

It will be seen that over 80% of the factories in our area and in the country as a whole employ between one and 25 people. These, and most subsequent figures, relate to the 48 factories where we obtained an interview. We do not know exactly how many work people were employed in the two firms where interviews were not obtained. We knew, however, that they had few employees and their exclusion from our figures is not likely to alter the general pattern.

The main types of industry represented and the percentage of workers employed in them in our area and in Great Britain as a whole are shown in Table 2. A list of the major products of the factories

surveyed is given in Appendix II. The diversity of work done in these small factories in one area is noteworthy.

TABLE 2

DISTRIBUTION OF FACTORIES AND WORKERS BY TYPE OF INDUSTRY IN SURVEY AREA AND GREAT BRITAIN, 1958

Manufacturing Industry Groups*	Survey Area		Great Britain
	Factories No.	Workers	Workers (%)
Chemical and allied	—	— —	6
Metal engineering, vehicles, electrical	20	420 (42%)	48
Textiles, clothing, leather	6	70 (7%)	17
Food, drink, tobacco	4	122 (12%)	9
Precision and musical instruments, wood and furniture	8	228 (23%)	5
Other	10	164 (16%)	15
All manufacturing industries	48	1,006 100	100 No. approximately 9 million

* Based on an amalgamation of some of the groups listed in the standard industrial classification (*Ministry of Labour Gazette*, 1958).

The original purpose and estimated age of the buildings now used as factories are shown in Table 3.

TABLE 3

ORIGINAL PURPOSE AND DATE OF CONSTRUCTION OF PREMISES

Original Purpose of Present Premises	No.	Date of Construction of Present Premises	No.
Factory	18		
Dwelling	7	Pre 1918	40
Railway arch	3		
Outhouse	3	1919-1945	2
Shop	2		
Mixed	10	Post 1945	6
Other	5		
Total	48	Total	48

Only 18 of our firms were operating in premises originally built as factories. All the rest were using converted premises of one sort or another, including railway arches, shops, garages, and private houses. They formed a motley collection of buildings of all shapes and sizes. Moreover, 40 out of 48 firms were operating in premises built before 1918. Only six were in buildings of post-war vintage.

Inevitably, these factories face problems of a very different kind from those faced by the factories in the Slough Health Service, for example. Slough's factories were built mainly between the two world wars, while the industrial medical scheme at Harlow, a post-war new town, to take another example, caters for firms working in up-to-date premises, all built in the last six or seven years.

Our factories, on the other hand, were distinguished by their venerable age and their makeshift character; decay was more prevalent than construction. But in this respect we did not feel that our area was necessarily unlike many other urban areas in England. Some of the different types of factory building represented in our survey are illustrated in Figs. 1-7.

Sanitary and Washing Facilities.—The Factories Act, 1937, lays down that "sufficient and suitable conveniences must be provided, kept clean and efficiently lighted" and that "where both sexes are employed, there must be separate accommodation for each sex". The Act also calls for "adequate and suitable facilities for washing, conveniently accessible, provided with soap and clean towels or other suitable means of cleaning and drying".

The problem, of course, is to agree on what is regarded as "sufficient", "convenient", or "adequate". Opinions on these matters are likely to differ among different sections of the community, not to speak of differences between individual doctors. However, in eight factories the three observers agreed that by no stretch of the imagination could the sanitary accommodation provided be described as either "suitable" or "clean", and in three instances the firms concerned had no lavatory or urinal at all. We suspect that we have over- rather than under-estimated the amount of lavatory accommodation and washing facilities, because it was evident that some firms shared them. For example, the five factories around a courtyard (Fig. 5) where there was one urinal, claimed it as their own.

As for washing facilities, only one small firm was without so much as a tap and basin; the rest complied with the law in varying degrees. One employer, with an eye to costs, and as a result of a court case, had ingeniously installed a wooden trough, fed by overflow hot water from a dirty tank, for his workers to wash in. Two other firms allowed their workers to share this amenity.

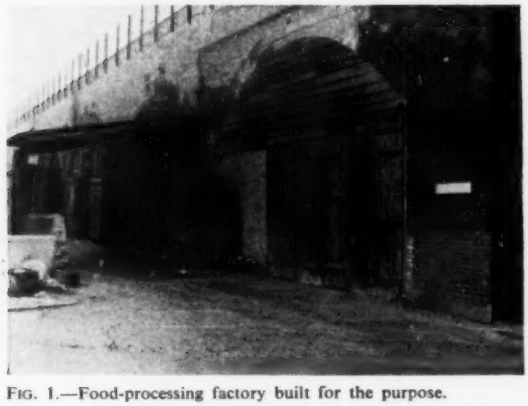
We were not able to obtain illustrative photographs of inadequate facilities. Fig. 8 is an example of facilities such as we met quite frequently and which we considered adequate, if not desirable. It shows the separate accommodation for women in a building which housed a toymaker's shop, an electrical firm, and a metal working shop.

Environmental Factors.—First, we assessed certain environmental conditions—temperature and ventilation, lighting, noise, cleanliness—which are believed to have an effect on general health and well being. Secondly, we listed those manufacturing operations and processes known to be associated with certain specific industrial diseases and accidents.

1

2

3



4

FIG. 1.—Food-processing factory built for the purpose.

FIG. 2.—Converted premises consisting of a private house, a shop, a factory.

FIG. 3.—A joinery factory occupying three railway arches.

FIG. 4.—Railway arch factories.

The accurate assessment of any one environmental factor requires frequent measurements with special instruments over a prolonged period of time. This was not attempted. What we did was to ask each of the three observers to record, independently of each other, whether they regarded a particular environmental factor as sufficiently bad to be likely to have an adverse effect on the health of those exposed. Despite our attempts to obtain agreement on criteria, the standards expected by our observers, none of whom were experienced factory inspectors, varied. They were largely based on their previous experience in other health fields. We discarded, therefore, adverse reports by only one observer and included those where two or all three observers agreed that the conditions were unsatisfactory.

We were pleased to note that under the impressive heading *General Assessment of Layout and Efficiency of Plant and Machinery in relation to the Health of the Worker*, the authors of the Halifax report wrote:

> "After careful consideration the survey team came to the conclusion that little useful purpose could be served in tackling this most complex subject unless each process was dealt with separately. This would have taken far too long and could not be undertaken in a general survey."

With this conclusion our group agreed.

Overcrowding.—The legal requirement is that: "A factory shall not, while work is carried on, be so overcrowded as to cause risk of injury to the health of the persons employed therein." A minimum of 400 cubic feet per person is then given as the statutory requirement. Only one of the factories visited, a shirt maker employing 23 workers, was considered to be below this standard. The room was small and the machines close together. The girls sat in four rows facing each other and were surrounded by bales of cloth.

Temperature.—Temperature in all workrooms must be "reasonable" and where a substantial amount of time is spent sitting down, the temperature must be over 60°F. after the first hour. As a group, we were more than aware of the difficulties of assessing "reasonableness". Some of our members came from the tropics and had their first experience of snow while actually trudging round the area; others of us were thoroughly used to the draughts which the Englishman euphemistically refers to as "fresh air". But, after visiting these factories, some of us felt that it was the nature of the work rather than the comfort of the worker which was often the deciding factor in the matter of temperature. For example, pianos, it seems, prefer a warm, dry atmosphere and the piano factories, which we visited on a cold day, were comfortably

5

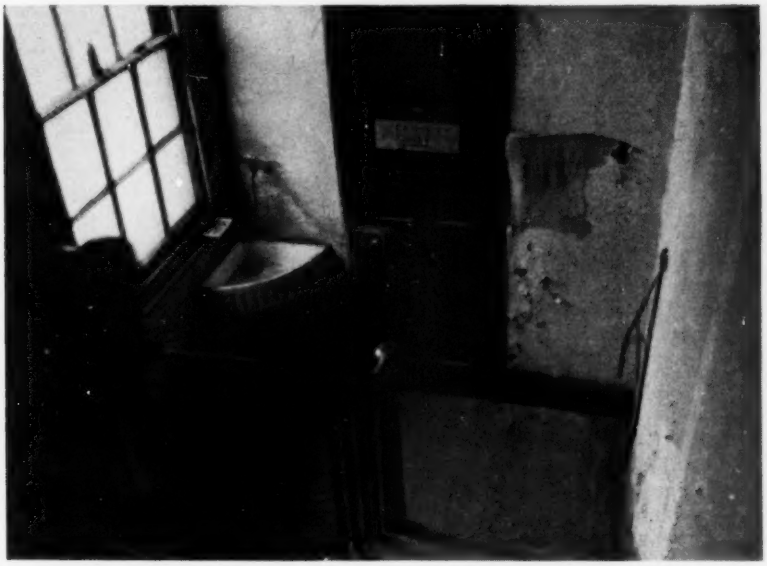
6

7

FIG. 5.—Courtyard on to which five factories open.

FIG. 6.—Nineteenth century factory building now occupied by four small firms.

FIG. 7.—A factory entrance.



8

FIG. 8.—"Separate accommodation"

warm. The fish curer's and glass merchant's factories, however, which we visited on the same day, struck us as decidedly cold.

Noise.—Noise is not mentioned in the Factories Acts and no statutory limits have, so far, been produced. Compensation for hearing loss has only been claimed at Common Law. In one or other part of three factories—a furniture works, a pianoforte part works, and a sign manufacturer's shop—the noise was considered "excessive". In the last, we could not hear an operator's voice above the noise of his machine; but he told us that he did not mind the noise because "I've got used to it".

Lighting.—The provision of "sufficient and suitable" lighting, whether natural or artificial, in every part of the factory in which persons are working or passing was a new requirement in the 1937 Factories Act. We assessed the existing lighting under two headings, "at the work bench" and "on the stairs". We did not see any gross instance of bad lighting at the work benches. On several occasions we thought that there might have been some glare from unshaded electric lights but we did not make a single judgment of inadequacy. We were struck by the number of occasions on which we saw filthy windows. The dirt and dust of ages coated many of them, including those in an electro-plating factory in which broken glass had not been replaced but the holes filled up with cardboard and newspaper.

We were rather more critical of lighting on stairs and passageways. We recorded nine instances of bad lighting. In one case, where the stairway was in continuous use, the stairs were narrow, rickety and steep, the handrail was broken, and the only lighting was a low wattage bulb high up on the ceiling.

Cleanliness and Tidiness.—The law requires that every factory shall be kept in a clean state and specifies that "accumulations of dirt and refuse must be removed daily from floors and benches of workrooms and from the staircases and passages"; that "the floor of the workroom must be cleaned at least once a week by washing or, if it is effective and suitable, by sweeping or other method" and contains provisions for "cleaning or whitewashing or colourwashing walls, tops of rooms, passages, and staircases at least once every 14 months". The last requirement is not enforced in non-power factories where less than 10 persons are employed. There are no legal standards for tidiness, but this was also considered, more because of its possible relation to accidents than to disease.

Our assessments were made on overall conditions without specific reference to benches, floors or walls. Ten factories (22%) were considered unsatisfactory. These were mainly the smaller factories, seven of them having less than six employers each. Although 22% of the factories were unsatisfactory in this respect, they only accounted for 8% of the employees.

Among the dirty places that we saw was a small shoemaker's shop where fragments of the employees' lunch collected among the days-old accumulation of odd pieces of leather; there was also a wash-

FIG. 9.—An accumulation of dust from grinding.

FIG. 10.—Office, workshop, or canteen?

FIG. 11.—Ingots and junk stacked around a furnace.

FIG. 12.—An electro-plating shop.

11 (*above*)
12 (*below*)

room used by the workers as a kitchen but never cleaned as far as we could see. "Untidy" places, on the other hand, included one where the floor space was covered with iron and metal ingots stacked one on top of each other, higgledy-piggledy. One worker told us nonchalantly that he quite frequently had an ingot dropped on his toe but that you "don't have to worry as nails come off and grow again". Another factory was described by one observer as being "untidy, dangerous, full of half-made furniture blocking the passageways, and presenting great fire hazards".

In conclusion, and very much in general, it would

be fair to say that we saw among our 48 factories some conditions which we thought could hardly be bettered, considering the age of the buildings, and others which, from the standpoint of dirt and the accumulation of rubbish could scarcely have been worse (Figs. 9-12).

Hazards.—It is generally, although by no means always, true that in small factories each man carries out many varied operations so that, even if one of the operations is potentially dangerous, his exposure to it is likely to be intermittent. We tried to identify those operations and machines known to cause trouble in manufacturing industry, on the assumption that, even if only used intermittently, they were still potentially dangerous and should be subject to inspection. As a rule we did not attempt to make any decision as to whether the necessary precautions for safe usage were adequate, although we did note some instances where we were convinced that safeguards were inadequate. Questions about protective clothing were asked in order to find out whether dangers were at least recognized.

Operations Involving Production of Dust or Fume.—Altogether, 35 operations producing dust or fume were noted. Paint-spraying was done in eight factories, electro-plating (using chrome, cyanide, etc.) in four, degreasing (with trichlorethylene) in two, shot-blasting in one, various forms of metal grinding and polishing in eight. Diesel fumes, cotton dust, and, incidentally, the smell of smoked salmon and roasted peanuts were noted in others.

In some instances these hazards were recognized and local exhaust ventilation was provided. Where it was present, however, it did not always appear efficient. In one case paint was still being deposited on the back of the man who was spraying. In other cases, masks were worn, sometimes round the neck and sometimes made out of a rag and held in place with a rubber band.

Chemicals Used.—The list of chemicals used was undoubtedly incomplete, but in 30 factories the use of potentially dangerous chemicals was noted.

Caustic acids and alkalis, which require safe handling techniques to avoid the risk of burns, were noted 13 times. Carbon tetrachloride, a dangerous narcotic and liver poison, was used in three factories. Other chemicals capable of causing the commonest of prescribed industrial diseases, dermatitis, included naphthalene, detergents, mineral oils, kerosene, and many others.

Gloves were occasionally provided, but more often such remarks as, "we are careful, you know", or "we sort of get used to it", were made. One man obliged by dipping his bare arm into a fuming electro-plating tank, commenting as he wiped the liquid off on his trousers, "It stings a bit, but does not bother me. I'm immune."

Power-driven Machinery.—Thirty-nine (80%) of the 48 factories questioned were classed as "using mechanical power" and the machines found in them are shown in Table 4.

TABLE 4

TYPES OF POWER-DRIVEN MACHINERY USED AND THE NUMBER OF FACTORIES IN WHICH THEY WERE FOUND

Machine	No. of Factories in which Present
Grinding wheels	23
Drilling machines	21
Circular saws	12
Guillotines	12
Power presses	10
Cranes or hoists	9
Planing or sanding machines	6
Metal lathes	4

Most of these machines were well guarded and often only used by experienced craftsmen. However, there were instances where sufficient precautions were not taken. In one furniture factory, for example, there were four inadequately guarded circular saws, all running simultaneously, in a crowded workshop.

Accidents.—The annual report of the Chief Inspector of Factories for 1956 (Minister of Labour and National Service, 1958) gives the total number of accidents occurring in factories during the year as 160,116. The estimated factory population was 7,850,000. This gives an accident rate of between 20 and 21 per 1,000 workers employed per year. The commonest causes of accident were the handling of goods (27%), power-driven machinery (15%), persons falling (14%), stepping on or striking against objects (8%), struck by falling objects (8%), and use of hand tools (8). In the tabulation of power-driven machinery accidents by cause, two-thirds of them are to be found in an unclassified group. However, the two types of machinery causing half the classified accidents—lifting gear and circular saws—were well represented among our small factories.

All the potential causes of accidents listed by the Chief Inspector were present, therefore, to a greater or lesser extent in the factories in our area; and accidents did occur. An examination of the factory accident books revealed 17 accidents in the 12 months before our enquiry, giving an accident rate of approximately 17 per 1,000 employed, or just below the national accident rate. However, 21 (44%) of our factories, including all the smallest, had no accident book. It might consequently be fairer to

relate the accidents only to those factories which had books, in which case the accident rate would have been nearer to the national figure.

The effect of the size of the working group on its accident rate—the smaller the group the lower the rate—(Acton Society Trust, 1953) is clearly not the only reason for the low rates for small factories given in the report of the Chief Inspector of Factories for 1954 (Minister of Labour and National Service, 1955). Inadequate or non-existent records contribute to this result.

On the other hand, we felt that the small firms in this area did attract a type of employee who was less likely to have a serious accident than did the large firms. For example, we gained the impression that the craftsman, and particularly the individualist, who chooses to work "on his own" and can turn his hand expertly to a number of trades, was more strongly represented than we would have expected in larger firms. As a result of his interest in work and the closer relationships between employer and employed which are possible in small firms, such a man is, perhaps, more willing to put up with unsatisfactory physical surroundings than other workers. He may also be less liable to accidents, even if hazards are greater, because he is less easily distracted from his work, and because his competence ranges over a wider variety of operations.

First Aid.—Every factory establishment, however small, is required under the Factories Act, 1937, to make some provision to cope with accidents which may take place at work. This means first and foremost that it must have a first-aid box.

The first-aid box must contain only appliances or requisites for first aid. For factories employing fewer than 10 workers, the minimum contents of the box must be (*a*) sterile dressings, (*b*) iodine or gentian violet, (*c*) sal volatile. As the number of employees increases, so the firm is required to increase the number of dressings and the range of appliances.

In 43 of the 48 factories visited we saw a first-aid box. In a further two we were told one existed, but we did not actually see it, and in three there was no box at all. All but one of these boxes contained some antiseptic; fortunately, perhaps, this was not often iodine. Three boxes contained no sterile dressings. On the whole, we felt that there was a good deal to be desired where first-aid equipment was concerned. No fewer than 12 out of the 43 factories were unanimously considered to be deficient in this respect by the three observers.

Moreover, we found that managements sometimes kept supplies locked away on the grounds that, if they were kept in boxes, they would be stolen. One works manager, who told us this, was unable to find the key to the drawer in which, he assured us, the sterile dressings and antiseptics were kept.

The Factories Act also insists that the box should be under the control of a responsible person who, if more than 50 people are employed, must be trained. In our area, it seemed to us that there was a so-called responsible person in rather less than half of the firms and, of the six firms with more than 50 employees, only three had men who could by any stretch of the imagination be described as trained. In short, we gathered much the same kind of impression as the Halifax surveyors who stated that "it was largely a matter of luck rather than planning that first-aiders were available".

Provision of Health Services.—We were also interested to see whether firms made any provision beyond those required by law. We found very little. Only one establishment, the bus depot, had a special treatment room. No factory employed a nurse, either full or part-time. Three firms out of the 48 (the three largest) had definite arrangements with doctors. These were to examine new employees, and, at the bus depot, the responsibility of the medical officer extended to interest in the environment more generally.

The most common form of voluntary provision beyond the minimum required by law was the dispensing of aspirins. Thirty firms kept these in the first-aid box and eight said that they were asked for frequently.

We wanted to know what firms were likely to do in case of a medical emergency. We asked them, therefore, what they would do if one of their employees were to cut himself badly. Thirty-nine replied promptly that they would take the worker to hospital as quickly as they could. Seven would have called an ambulance rather than take the worker to hospital themselves. Only two would have called on a local general practitioner for help.

The hospital facilities for the area were unusual. There were two large general hospitals, both with casualty departments, about three-quarters of a mile and a mile away respectively from the centre of our area. One of these hospitals, however, had a casualty and out-patient department in premises situated even nearer, that is within seven to 12 minutes' walk from any part of our area. This department dealt only with patients who came on their own; ambulance cases were taken to the main hospital. In the local casualty department a doctor and nursing staff were on duty 24 hours a day. Approximately 100 patients were seen each day and the waiting period to see a doctor was estimated to be half an hour and to see a nurse 10 minutes.

In order to estimate roughly the proportion of cases dealt with at this centre that were "industrial" rather than "domestic", a sample of entries in the daily register was analysed. The "industrial" cases were taken to be the bulk of those between the ages of 16 and 65 who attended between 8.30 a.m. and 6.30 p.m. In nearly all these cases where Christian names were given they appeared to be males. Seventy per cent of the cases were in this group. The causes for attendance among the group were injuries to fingers and hands, 30%; other injuries, 20%; burns, 10 %; miscellaneous conditions, 40%. The Casualty Officer thought that many of the injuries were so trivial that they could have been dealt with by a good first-aider at the workplace of the individual concerned.

There was no doubt, however, that the firms thought these arrangements to call on the local casualty department entirely adequate and appropriate. Only one manager thought that a special industrial service with a doctor available and a nurse to do regular dressings might be desirable. The others usually argued that accidents were too infrequent to justify any special services.

Official Inspections.—All factories are subject to inspection in order to see that they comply with the Factories Acts and other regulations concerning the health and safety of employees.

Various government departments and local authorities have different people with statutory duties to perform in connexion with factories. Table 5 shows who these are and how often the factory owners said that they visited their factories.

TABLE 5

FREQUENCY OF VISITS TO 48 FACTORIES BY GOVERNMENT AND LOCAL AUTHORITY OFFICIALS

Officials	Number of Visits			
	Never	Visits in 1957		
		0	1	2+
Local authority health inspector	5	1	24	18
Medical officer of health	39	4	3	2
District factory inspector	13	4	22	9
Appointed factory doctor	39	7	1	1
Medical inspector of factories	45	3	—	—
Alkali inspector	45	3	—	—

The local authority health inspector visits all factories to inspect the sanitary arrangements and canteens where they exist. He has special duties in food processing factories. He was the most frequent visitor in the factories in our area, having visited almost every factory at least once in the last year. In the borough as a whole, three health inspectors spend nearly all their time visiting factories. They have to cover over 2,000 factories between them.

The medical officer of health would normally not carry out any routine inspection; but some medical officers like to know what goes on in the factories in their area. Nine of our factories said that they had been visited by the medical officer of health, often in connexion with teaching students. These included all the food processing firms.

The district factory inspector with an assistant covers an area, of which the borough is only a part, in which there are about 3,000 factories. These inspectors had visited about half the factories we saw during the past year. Thirteen of our factory proprietors, however, thought they had never had a visit from them.

The appointed factory doctor, whose job it is to examine new recruits aged 16-18 and those engaged in dangerous trades, was said to have visited only two factories. It should be pointed out, however, that some firms sent their young workers to his consulting rooms for examination. The area we surveyed was only a part of the area he covered. In all he made some 700 examinations of young workers during a year, detecting significant abnormalities in less than 1%. The medical inspector, who is one of only 15 in the country as a whole, and the alkali inspector, who today is concerned largely with smoke abatement, had not visited the factories in the area during the last year.

It was abundantly clear that the small firms were often confused by the duties and powers of their different visitors. One owner, when asked whether he had been visited by the alkali inspector, told us that he could not remember any such gentleman, but that he was so pestered by so many inspectors of all sorts that he could not believe that he would have been missed. On the other hand, we discovered one firm in which the factory inspector had found many faults on numerous occasions. To avoid the expense of complying with his requirements the manager took his two skilled employees into partnership and sacked the boy. As no one was then employed the premises ceased technically to be a factory. When the fuss had died down the boy was taken on again, but was liable to instant dismissal or promotion to full partnership should the factory inspector reappear.

It is only fair to conclude by saying that the various inspectors whom we met were fully aware of their inability to meet all the needs in the area.

Discussion

Our investigation can be described as a preliminary reconnoitre of a field about which remarkably little has been written. Our aim was two-fold; first, to identify the health needs of small factories, and second, to estimate how far

these needs were being met either by services which the firms themselves provided or by those available in the neighbourhood. We had neither the time nor the resources to make it a thorough or authoritative survey of all the factors involved; moreover, there was a large element of Hobson's choice in the selection of an area in which the issues could be investigated. Thus, we recognized that the area surveyed, like most central London boroughs, was rather better served by hospitals than most provincial industrial centres. In addition, we discovered that it had on its doorstep a special branch casualty department capable of dealing expeditiously with minor industrial ailments and accidents. In other respects, however, it probably resembled many areas of mixed industrial and residential development near the centre of industrial towns. Despite the limitations, therefore, we feel that it is worthwhile, not only to state our findings, but also to suggest some of the conclusions which we have drawn from them.

Health needs may be roughly divided into therapeutic and preventive. The services which meet the first kind of need are directed to the individual who has an accident or falls ill, whereas the preventive services are predominantly concerned with the control of the environment, although they too provide some services to individuals, for example, through routine examination or mass miniature radiography.

In the area investigated, the main shortcoming in the therapeutic health services was the poor standard of first aid. In many firms the equipment provided and the training of those in charge could, by no stretch of the imagination, be considered satisfactory. Improvement was urgently needed. The question is, how such a drastic improvement can be brought about. We have little doubt that the most effective way of securing a reasonable standard of first aid in the small firms would be to increase inspection. The managements' own enlightened self-interest is not likely to extend far enough to permit the expenditure of much time and money on the necessary training and equipment without a good deal of pressure from an inspectorate. It would be easier to enforce the law if the requirements concerning the contents of first-aid boxes were amended and brought into line with current medical practice. The existing regulations* still call for the provision of iodine, an antiseptic which can be positively harmful, and sal volatile, which can seldom be of much use today when young women workers do not often suffer from either hysterical fainting fits or from corsets too tightly laced.

* New regulations, the First-Aid Boxes in Factories Order 1959, Statutory Instrument 1959 No. 906, have been published since this was written and will come into force on January 1, 1960.

The casualty service provided by the local branch of a general hospital was adequate, in our opinion, to meet the needs of local industry. Managements knew of its existence, and, both in emergencies and for subsequent dressings, it was able to cope with the volume of casualty work in the locality. In this area, therefore, we agreed that there was no place for an additional industrial clinic and casualty service. In areas less well served by hospitals, however, the need might be great. Certainly, general practitioners, as at present organized, would not be able to deal adequately with these needs.

Theoretically, an appointed factory doctor responsible for conducting the routine examination of young workers and the periodic examination of some older employees, could have a considerable influence on the firms' ideas and attitudes concerning the health of their workers. In practice, however, we felt that this influence was not exercised in the very small firms. The appointed factory doctor seldom visited any of the small factories, and could not, therefore, get to know the employers or see for himself the conditions under which juveniles worked. Moreover, some employers were not referring their young workers for examination.

Turning from the therapeutic requirements of individuals to the needs of all workers for a healthy working environment, we saw many working in conditions which were sufficient to undermine any complacency. Although we saw some factories where conditions seemed entirely satisfactory, there were several instances where the term "slum factory" was not a misnomer.

The dirt and squalor which led us to describe a factory as a "slum" were often inevitable concomitants of the age and unsatisfactory nature of the premises. Even the most willing management with the best medical advice at its disposal would be fighting a losing battle in such circumstances. But the problem in these factories is aggravated, because it is often the small undertakings with narrow profit margins which occupy such premises.

In the worst cases, real improvement is almost impossible without rebuilding. In this sense, we were pleased that some of the small factories that we visited were shortly to be demolished as part of a slum clearance area. Many of these need to be in the neighbourhood of the larger factories which they often serve as subcontractors. In the area surveyed, for example, an electro-plating factory and a metal-working shop, amongst others, were engaged in subcontract work for other nearby firms. Rehousing them in the industrial areas of suburbs of new towns is, therefore, often impracticable unless the parent industry moves too. Even in this case domestic considerations might make the owners of

small businesses reluctant to leave a district in which their families and those of their employees may have lived for generations.

In some areas, notably Birmingham and London, local authorities, recognizing the needs of small factories, have built large blocks of "flatted factories" or "unit workshops" in slum clearance areas. It is still too soon to say how successful they have been but it is clear that such schemes, even if successful, will take a long time to make much impression on the 200,000 small factories in the country.

While wholesale rehousing would form part of an optimum solution, much could be done to improve the working environment without such drastic measures. First, many of the deficiencies of the general environment could be remedied if managements could be cajoled into spending more money on cleaning and tidying, on heating, on the lighting of stairs and passageways, and on the provision of up-to-date lavatories and wash basins. Secondly, specific accident or disease hazards could be reduced or eliminated if both managements and men could be persuaded that their own interests would be best served by observing the safety regulations of the Factories Acts.

In the large firm, these objectives are often achieved because a firm with a reputation to maintain does not wish to risk a prosecution for failing to comply with the Factories Acts. Moreover, trade union representatives will exert some pressure, especially at a time of full employment. But managements in large firms have a further motive for taking steps to provide optimum working conditions—enlightened self-interest. Crudely stated, they are prepared to employ medical staff and technical advisers because they know that attention to the hazards of the working environment pays.

There is no doubt that industrial medical services covering small factories could accomplish much; but we consider it quite unrealistic in an area such as that which we surveyed to suppose that existing small managements would be prepared to join with neighbouring firms to introduce such a scheme. It is not only that small firms are much less sophisticated than their larger counterparts. It is also that existing industrial health services, whether run by companies themselves or on a local cooperative basis as at Slough and Harlow, have almost always grown from a preliminary recognition of the need for therapeutic services. Only when these were well established was it possible to extend the concept to cover indirect control of the health of the worker by control of his environment. In the area we surveyed, casualty work and treatment of minor ailments are already adequately covered by the special out-patient and casualty department of the local general hospital. We do not think it likely that firms, who consider that their needs are satisfactorily covered from this point of view, would rush into a venture of which the advantages are much less obvious.

In these circumstances, the only practicable way of securing radical improvements in the working environment seemed to us to be through an improved system of statutory inspection.

It is notorious that the number of factory inspectors throughout the country is still inadequate to ensure the regular inspection of all factory premises. Certainly, in the area surveyed, the district factory inspector had not been able to visit nearly half the firms within the last 12 months. The local authority health inspector had visited more firms to carry out his duties in respect of sanitation, canteens, and food handling.

It was our impression, however, that the functions and competence of the two types of inspector were often confused in the minds of many proprietors. In many respects the proprietor of the small firm is like the head of a domestic household, and his factory or workshop is often more akin to the home workroom than it is to the workshop of a large factory. It has been suggested that a plethora of social workers, all concerned to help or cajole a "problem" family into conformity, is likely to confuse rather than clarify matters for the family. We feel that it is legitimate to draw a parallel between this example from the domestic scene and the situation in the small factory. All the premises we visited were technically factories according to the law; but we were constantly aware of the continuum which exists from the wage earner exploiting a hobby in his spare time at home, through the family partnership, the individual with a few hand-picked friends—all working directors—to the man who, by virtue of the one or two assistants he employs, is deemed to be running a factory. It was our impression that all these types of productive enterprise, only one of which is called a factory, have much more in common with each other than has the factory which employs less than a dozen workers with the factory employing a hundred or more.

If our impression is correct, it may be more fruitful to think in terms of a system of inspection which would be appropriate in the home rather than in the large factory. Above all, inspection for the small factory calls for simplicity. The small proprietor has often to be administrator, salesman, buyer, foreman, and worker all in one. For this reason he is the natural enemy of bureaucracy and unnecessary "paper work". If his relations with the statutory authorities could be conducted through

a single individual who could get to know the business and its problems well, there would be a much better chance of securing lasting improvements in the working environment and first-aid arrangements.

It would be premature on the basis of such a small survey to discuss how such an inspectorate could be formed. There are certain attractions about the view that the local health authorities' inspectors, who already have statutory responsibility for sanitation and food handling, should discharge the duties of the Ministry of Labour Factory Inspector as well; but it could equally be argued that the factory inspectors' skills could not quickly or readily be imparted to the health inspectors whose training is not primarily concerned with occupational hazards. There is, however, a strong case for suggesting that a fresh approach to the needs of workers in small factories is required.

Finally, it is our contention that, at a time when the extension of occupational health services and the development of occupational health laboratories are being planned, there is need for a great deal more information about the needs of small factories. Our own limited survey tends to confirm those findings of the Halifax Survey (1958) which were published. In both areas, there was ground for real concern about the adequacy of the safeguards for the health of the worker. If the best solution for the problems uncovered in such surveys is to be found, it is imperative that as much information as possible should reach the public. Only if the medical and lay publics are adequately informed can they contribute to the solution.

We would like to record our thanks to the Medical Officer of Health for the metropolitan borough in which the survey was done, and to those members of his staff whose assistance in the initial stages of our enquiry was most valuable. We would also like to thank the District Factory Inspector for the area concerned, and the managements of the 48 factories who generously answered our questions and allowed us to take photographs. The photographs in this report were taken by Drs. R. O. M. Jones, R. H. Strudwick, and E. C. Cummings.

References

Acton Society Trust (1953). *Size and Morale*. London.
Ministry of Labour Gazette, **66**, No. 4, p. 146 (1958).
Ministry of Labour and National Service (1955). Annual Report of the Chief Inspector of Factories for the year 1954. H.M.S.O., London.
—— (1958). Annual Report of the Chief Inspector of Factories for 1956.
—— (1958). Industrial Health. A Survey in Halifax. H.M.S.O., London.
Slough Industrial Health Service (1957). Tenth Annual Report 1956-1957.
Taylor, S. (1958). *Practitioner*, **181**. 133.

APPENDIX I

Medical Services for Small Factories

CONFIDENTIAL
Correct Answers should be ringed

1. No..... Date...../...../ .....
2. Observer .....
3. Name of firm.....
4. Address .....
5. Description .....
6. Power.....1. Non-power..... 2.
7. Name of person interviewed.....
8. Position held.....
9.

Personnel	Male		Female		Total
	−18	18+	−18	18+	
Manual					
Clerical					
Foremen and Managers					
Total working on premises					

10. Year firm established in present premises — pre-1918...1; 1919-45 ...2; 19 ___ .. 3
11. *Premises.* Fabric — Brick .....1; Other (specify)...2; .....
12. ,, Age — pre-1918...1; 1919-45 .. 2; 19 ___ .. 3
13. ,, Storeys occupied. B. G. 1. 2. 3. 4+
14. ,, Original purpose
    Dwelling .....1 Shop 2
    Outhouse .....3 Factory 4
    Warehouse .. 5 Railway arch 6
    Other (specify) 7
15. *Dust and Fume Operations*
    Paint spraying ..... Yes No....1
    Metal buffing ..... Yes No....2
    Sand blasting ..... Yes No....3
    Electro-plating ..... Yes No....4
    Degreasing tank ..... Yes No... 5
    Others (specify)
    6

16. *Chemicals Used*
    - Caustic acid/alkali ..... Yes/No....1
    - Carbon tetrachloride ..... Yes/No....2
    - Others (namely) ..... Yes/No....3

17. *Machinery*
    - Circular saw ..... Yes/No....1
    - Guillotine ..... Yes/No....2
    - Drilling machine ..... Yes/No....3
    - Power press ..... Yes/No....4
    - Grinding wheel ..... Yes/No....5
    - Crane ..... Yes/No....6
    - Others (namely) 7

18. *Protective Clothing Supplied*
    - Goggles ..... Yes/No....1
    - Gloves ..... Yes/No....2
    - Masks ..... Yes/No....3
    - Aprons ..... Yes/No....4
    - Boots ..... Yes/No....5
    - Others (namely) 6

19. *Sanitation*
    - (*a*) No. of W.C.s _____
    - (*b*) No. of urinals _____
    - (*c*) No. of washbasins _____
    - (*d*) Supplied with hot water? ..... Yes/No....1
      ,, ,, soap?..... Yes/No....2
      ,, ,, towel? ..... Yes/No....3

Medical Personnel available to firm

20. Doctor ..... Yes/No....1
    IF YES
    - Visits: Regularly .....2; Irregularly .....3; Never 4
    - Purpose: Accidents .....5; Exam. new entrants .....6; Routine exam. .....7; Special exam. .....8; Other (namely) 9
    - Payment: Retaining fee .....1; Service fee ..... E

21. Nurse ..... Yes/No....1
    IF YES
    - Full-time.....2
    - Part-time.....3
    - (Hours per week) _____
    - S.R.N.....4
    - Assistant 5

22. First-aider? ..... Yes/No... 1
    IF YES Trained? ..... Yes/No....2
    Nature of training .....
    Approx. date .....
    Position in firm .....

23. *First-aid equipment*
    - (*a*) Special room?..... Yes/No.
    - (*b*) Couch? ..... Yes/No.
    - (*c*) Box? ..... Yes/No.
    - (*d*) *If yes* does it contain
      antiseptic? ..... Yes/No....1
      sterile dressing?..... Yes/No....2

24. (*a*) Are aspirins available? ..... Yes/No.
    (*b*) *If yes* are they frequently dispensed to employees? ..... Yes/No.

25. Did you have any accidents during 1957 which entailed more than 3 days' absence? ..... Yes/No.
    IF YES How many? .....
    What happened? .....
    .....
    Action taken .....
    .....

26. What would you do if one of your employees cut himself badly?
    - Never thought about it 1
    - Take to hospital 2
    - Call ambulance 3
    - Call local G.P. 4

    Verbatim.....
    .....

27. Do you consider your present first-aid arrangements adequate for your needs, or would you like a doctor available for emergencies, or a nurse to do regular dressings?
    - Quite satisfied with present needs 1
    - Would like doctor for emergencies 2
    - Would like nurse for dressings 3

28. (*a*) Have you got an accident book? Yes/No.
    (*b*) *If Yes* produced ..... Yes/No.
    (*c*) How many entries were made during 1957? ..... No. .....
    What were the most common types of injury?
    .....
    .....

29. What would you do if you thought one of your employees had become ill as a result of his work?
    Verbatim.....
    .....

30. What would you do if you thought that some substance or machine you wanted to use might be dangerous to health?
    Verbatim.....
    .....

31. Would you consider consulting a doctor in such circumstances? Yes/No....1
    The factory inspector? ..... Yes/No....2

Visits		Never	Visits in 1957			Purpose of Last Visit
			0	1	2+	
32.	I.A. health (sanitary) inspector	X	Y	1	2	
33.	M.O.H.	X	Y	1	2	
34.	Factory inspector	X	Y	1	2	
35.	Appointed factory doctor	X	Y	1	2	
36.	Medical inspector factory	X	Y	1	2	
37.	Alkali inspector	X	Y	1	2	

Enter only if reasonably sure of accurate information

Assessments

38. *First Aid Equipment*
Inadequate ..... Yes/No.

39. *Crowding*
Over-crowded ..... Yes/No.

40. *Temperature*
Excessively hot ..... Yes/No.
Excessively cold ..... Yes/No.

41. *Lighting at work benches*
Inadequate ..... Yes/No.

42. *Lighting on stairs, etc.*
Inadequate ..... Yes/No.

43. *Noise*
Excessive ..... Yes/No.

44. *Cleanliness* (general)
Dirty ..... Yes/No.

45. *Cleanliness* (W.C.)
Dirty ..... Yes/No.

Factory No......

46. *Tidiness*
Very untidy ..... Yes/No.

General Impressions of Visit
Hazard Notes, etc.

APPENDIX II

Classification of Industries in the Survey by Main Product or Activity

1. *Chemicals and Allied Trades:*
Nil

2. *Metal manufacture, Engineering, Shipbuilding, and Electrical Goods, Vehicles, Metal Goods not Elsewhere Specified*

Printing engineers	Metal workers
Spring makers	Metal spinners
Panel beaters	Coach builders
Radiator and car restorers	Ball bearings makers
Hospital equipment restorers	Sign manufacturers
Metal platers	Foundry
Radio parts	Screwmaker
Light engineering (2)	Metal merchant
Electrical repairers	Pen maker
	Ball pen makers

3. *Textiles, Leather, Leather Goods and Fur, Clothing*

Knitting	Shoemaker
Shirt maker	Skirt maker
Leather works (2)	

4. *Food, Drink, and Tobacco*

Fish curers	Peanut roasters
Imitation cream manufacturers	Potato merchant

5. *Precision Instruments, Jewellery, etc., Manufacturers of Wood and Cork*

Furniture maker (2)	Wood merchant
Optical manufacturers	Piano manufacturer (2)
Cabinet maker	Piano parts manufacturer (2)
Wood polisher	

6. *Others*

Wallpaper printers	Artists' colourmen
Toy makers	Scrap and tyre depot
Bus depot	Printers
Transport depot (2)	Glass merchants
Advertising depot	

Brit. J. industr. Med., 1960, **17**, 25.

STUDIES ON THE NATURE OF SILICOSIS

A SUGGESTED MECHANISM OF FIBROGENESIS

BY

P. F. HOLT and C. W. WENT

From the Department of Chemistry, Reading University

(RECEIVED FOR PUBLICATION MARCH 10, 1959)

One theory which seeks to explain the production of fibrous tissue in silicosis postulates the interaction of collagen precursors with polysilicic acid. This stage has been questioned because it is doubtful whether polymerized silicic acid is normally formed when quartz dissolves in aqueous media. A mechanism by which silicic acid may be polymerized *in vivo* has been demonstrated by studying the properties of polyamide monolayers, which behave like collagen monolayers when spread on silicic acid substrates. The silicic acid which is adsorbed beneath the monolayer polymerizes when the polyamide films are subjected to pressure.

In fibrogenesis, the polysaccharides which are produced in large amounts may serve to prevent the premature agglomeration of the collagen units. Later, when the concentration of the polysaccharide is largely reduced, the polysaccharide may assist in aligning and cementing the units together to form fibres. The physiological process is probably reversible but, if silicic acid takes the role of the polysaccharide in this second stage, the building up of fibres is likely to be an irreversible process.

Defects of the solubility theory, which sought to explain the fibrogenesis caused by silica, were examined in earlier publications. An attempt was made to modify the theory and so to remove some of the obvious anomalies (Holt and Osborne, 1953a and b; Holt and Yates, 1954). The original solubility theory (for a review, see Holt, 1957) regarded the silicic acid, produced when a siliceous dust dissolves in the tissue fluids, as a cell poison. However, attempts to demonstrate the toxicity of silicic acid failed and none of the evidence on which the theory was based appears now to be valid. It seems certain that silicic acid in tissue fluids will not of itself initiate fibrosis. Silicic acid appears to be active only if it is liberated in the cytoplasm of a fibroblast.

The modified theory suggested that simple silicic acids were formed in the cytoplasm of the dust cells and that this, diffusing from the cells, reacted with collagen precursors in the same manner as mucopolysaccharides are believed to react in the formation of normal fibres, producing stabilized collagen. Since these ideas were published, certain investigations of a fundamental nature have been made, the results of which are relevant to this discussion. A part of this material, as a contribution to knowledge in pure chemistry, has already appeared (Holt and Bowcott, 1954; Clark, Holt, and Went, 1957; Clark and Holt, 1957). The evidence for the interaction of proteins with silicic acid was described and the difference between the behaviour of collagen and that of other proteins was emphasized. Other experimental results, more directly related to the problem of silicosis, are recorded here.

Silicosis is essentially a disease in which collagen, a normal constituent, is formed in the lung in abnormal quantities. When silica particles enter the lung they are taken up by monocytes which become fibroblasts. Collagen is synthesized by the fibroblast, in the first place probably as ultramicroscopic rods or even spheres of protein which pass through the cell wall and, outside the cell, coalesce to form collagen fibres. The process of fibre growth is, then, analogous to crystal formation.

Collagen is always associated with polysaccharides and their function is a subject of speculation. Originally the polysaccharides were thought to act as templates on which the protein fibres were built (Partridge, 1948). Certainly chondroitin sulphate, for example, can precipitate small fibres from a solution of collagen (Cohen, 1942). Collagen fibres can be precipitated by simpler means, for example, by changing the tonicity of a saline solution of collagen (Nageotte and Guyon, 1935). Later, it was

proved experimentally that polysaccharides will stabilize collagen fibres, retarding changes which normally occur on heating (Jackson, 1953, 1954). More recently (Holt and Went, 1956), the polysaccharide secreted with the collagen precursor was thought to prevent premature coalescence of the protein fibrils, the large molecules preventing the protein chains from aligning one with another and so retarding the crystallization of the collagen. A mechanism by which the hydroxyl groups of water, and presumably those of polysaccharides also, may be attached to the collagen surface has been described (Fraser and Macrae, 1959).

It is conceivable that the polysaccharides serve all these functions. The very large amounts which are secreted with the collagen could hardly fail to hinder the development of the fibres in the first place but the amount of the polysaccharides later decreases and it may then assist in the alignment of the fibrils and stabilize the fibres when formed.

It is becoming apparent that the normal pattern of many tissues always involves both protein and polysaccharides. The permeability of the tissue depends on the amount and the degree of polymerization of the polysaccharides; the permeability is increased by the degradation or removal of the polysaccharides by polysaccharases. Even the control of the water content of the organism by the kidney appears to involve this system (Ginetzinsky, 1958). The polysaccharide, hyaluronic acid, is reported to be the substance controlling the permeability of the tubules and the permeability is largely increased by hyaluronidase. A polysaccharide-polysaccharase system of control for the production of collagen fibres would not, then, constitute a novel system.

The following sequence might be involved in fibrogenesis when silica is absent. The response of the fibroblast to the stimulus is the production of the elementary units of the protein collagen, together with large amounts of polysaccharide. The polysaccharide prevents the immediate aggregation of the protein units and the protein-carbohydrate complex moves away from the cell. The polysaccharide is gradually removed by polysaccharases and eventually the fibrils, with a layer of adsorbed polysaccharide, align to form fibres. The polysaccharide then acts as a cement substance between the fibrils but its amount is steadily reduced until only a minimal amount—perhaps a monolayer—remains. This view of the formation of collagen fibres is in keeping with the observations, made by electron micrography, that the carbohydrate associated with reticulin fibres is on the surface but that it is more closely associated with the older, fully-developed collagen fibres (Schwarz, 1957).

When silicic acid polymerizes a macromolecular structure is produced which can combine with and stabilize collagen (Clark, 1955). The possibility was considered that polysilicic acid behaves like the polysaccharides in the process of fibrogenesis as it is found in silicosis. Formed by the dissolution of silica particles in the cytoplasm, silicic acid would not be produced in a concentration likely to retard the production of fibres, but polysaccharides are simultaneously formed in large amount (Curran, 1952, 1953) and may serve this purpose. Polysilicic acid might serve as a template, and it will certainly stabilize collagen fibres even more efficiently than polysaccharides. It is not, of course, removed by polysaccharases.

This explanation of fibrogenesis assumes the polymerization of the silicic acid which is produced by the dissolution of silica particles; but silica dissolves slowly in aqueous media and produces a very dilute solution. Holt and Yates (1954) suggested that, because of the very high concentration of fine particles and consequent large surface of silica in the aggregation of monocytes, sufficient silicic acid might be formed for polymerization to occur. However, Wheatley (1957) found no polysilicic acid in extracts of silica, although Sakabe, Hasegawa, and Yamada (1956) reported that polysilicic acid is so formed. Their observations were all made on the simple silica-water system.

Some biological systems are certainly capable of concentrating extremely dilute solutions of orthosilicic acid and from them can produce silica itself. It happens in some plants, which produce silica in their leaves. Diatoms (*Asterionella*) build silica structures from very dilute solutions and the amount of silica in the structure is independent of the concentration of silicic acid in the environment (Einsele and Grim, 1938) which may be as low as 0·2 mg. per litre (Lund, 1950). Geological flints, which are often the inside casts of sea organisms, show that a mechanism exists by which even the trace of silicic acid in sea water can be concentrated to produce large masses of silica. In these cases the production of silica must entail the concentration and polymerization of orthosilicic acid in very dilute solutions, but by a process about which nothing is known and which has not been imitated *in vitro*.

Studies on the interaction of silicic acid with polyamide films and with proteins suggest that the concentration and polymerization of silicic acid could be effected by the collagen itself. The technique (Holt and Went, 1956) by which the studies are made consists in spreading a monomolecular layer of the polymer on saline and on a dilute solution of silicic acid. The films are slowly compressed. A graph drawn to illustrate the relation between the

applied pressure and the area of the film has a shape which is characteristic of the type of material. The shape of the curve may be altered if the silicic acid in the substrate interacts with the protein. The conditions under which silicic acid interacts with various proteins have been described (Holt and Bowcott, 1954; Clark *et al.*, 1957; Holt and Went, 1956).

Polyamides make excellent simplified protein models. They possess a sequence of peptide links separated by hydrocarbon chains and provide a structure similar to a protein backbone without the complication given by side chains.

The structures may be compared thus:

Polyamide . . .
$$-NHCO-(CH_2)_n-CONH-(CH_2)_n-$$
Protein . . .
$$-CONH-CHR-CONH-CHR-$$
R = amino-acid residue.
(Alternate peptide links are reversed in most polyamides.)

They are readily available and solutions of suitable concentration can be made much more easily than from collagen. Films of polyamides give force/area curves which are shallow, resembling those of collagen rather than those of most other proteins. In this study, polyamide films were used, the work previously published having shown the similarity in behaviour between polyamides and collagen films.

Experimental

Polyamides.—Solutions containing 0·01% of an amorphous copolymer, 66/6, 10/6 were spread from an ethanol + benzyl alcohol (3 : 1) solution.

Substrates.—To obviate complications due to polyvalent anions, substrates were not buffered. The *p*H was adjusted (HCl) before, and accurately measured after, each experiment. Polyamides were spread on 0·5 M NaCl.

Sodium silicate solutions (0·1 M) were either prepared by fusing pure vitreous silica (Thermal Syndicate Limited) with sodium carbonate (1 : 4) and dissolving the melt in water, or from sodium metasilicate. Solutions were treated with activated charcoal for 12 hours and filtered.

Silicic acid was prepared by adding 2 N HCl to the silicate solution. Polymerized silicic acid solutions, prepared by allowing 0·08 M silicic acid at *p*H 6·0 to stand up for up to 40 min. at 25-30°, were stabilized by acidifying with 2 N HCl to *p*H 1·5 to 2·0 and diluting to 0·05 M.

In solutions more dilute than 0·002 M orthosilicic acid does not polymerize. At higher concentrations at equilibrium, 0·002 M orthosilicic acid is always present and the excess is polymerized. Depolymerization of diluted polysilicic acid sols was found to be slow at 25°; below *p*H 6 little additional monomer was formed in, say, 10 minutes. The distribution of polymer sizes was, then, reasonably constant in all the prepolymerized substrates; they contained larger polymers and a range of smaller polymers down to orthosilicic acid.

Procedure.—Measurements of surface pressure were made with a Langmuir-Adam balance, using a waxed perspex trough (12.6 × 72 cm.). The polyamide was spread from solution by placing small drops from a glass micrometer syringe on the surface of the substrate, normally on an area of 2·2 m.²/mg. of polyamide.

Qualitative information about the viscosity was obtained by dusting films with talc and blowing on the surface.

Results and Discussion

When a polyamide film is formed on an aqueous salt solution and is then compressed, the relevant force/area curve is shallow (Fig. 1, curve A). If the sub-solution contains polysilicic acid in a concentra-

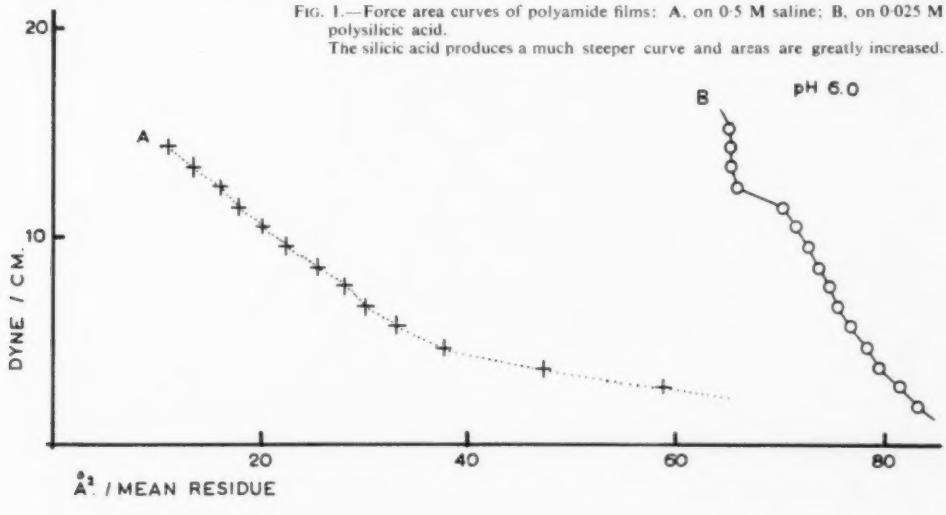


FIG. 1.—Force area curves of polyamide films: A, on 0·5 M saline; B, on 0·025 M polysilicic acid.
The silicic acid produces a much steeper curve and areas are greatly increased.

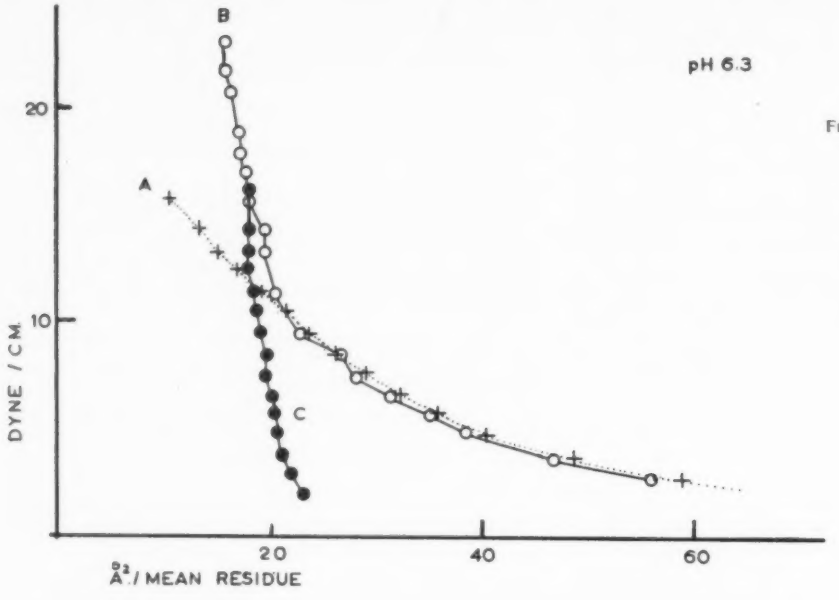
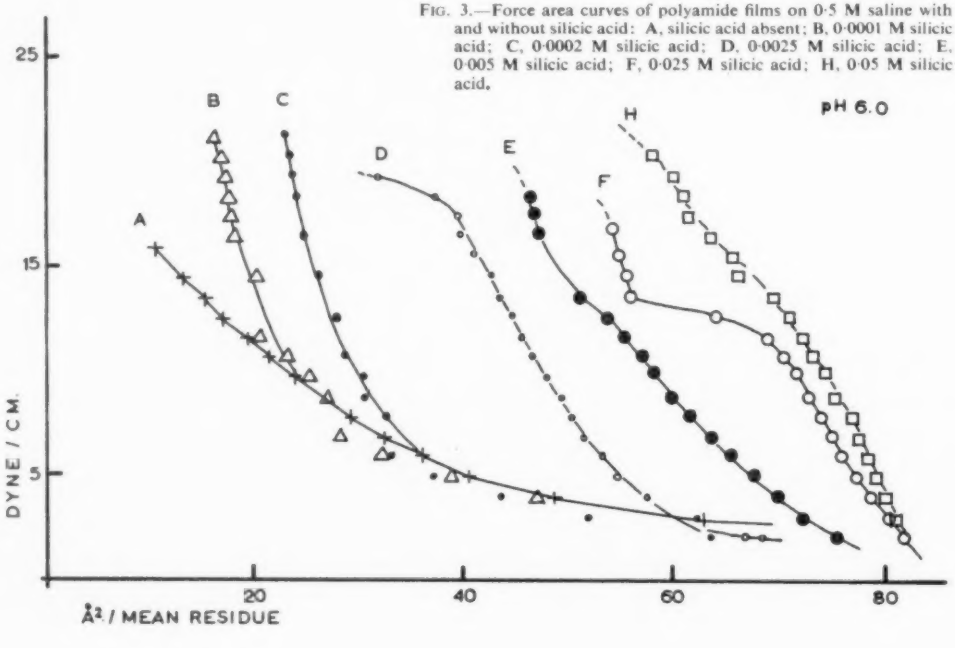


FIG. 2.—Force area curves of polyamide films: A, on 0·5 M saline; B, on 0·5 M saline + 0·0001 M silicic acid; C, same as B, second compression. The silicic acid is too dilute to affect the film until a pressure of 10 dyne/cm. is applied. The curve then rises steeply. Curve C shows that the protein-silicic acid complex is stable.

tion of say, 0·025 M, the form of the curve is altered. It rises steeply, and the change indicates that interaction has occurred and the film has been stabilized. Under these conditions the polysilicic acid particles which are adsorbed to the underside of the film approach one another so closely that interaction can occur between them, there is two-dimensional polymerization, and a permanent network forms. The film is said to be "tanned".

When the polyamide is spread on a solution of polysilicic acid diluted to 0·0001 M, the silicic acid apparently has no effect on the properties of the film at lower pressures, but above a force of about 10 dyne/cm., the curve rises steeply away from the

FIG. 3.—Force area curves of polyamide films on 0·5 M saline with and without silicic acid: A, silicic acid absent; B, 0·0001 M silicic acid; C, 0·0002 M silicic acid; D, 0·0025 M silicic acid; E, 0·005 M silicic acid; F, 0·025 M silicic acid; H, 0·05 M silicic acid.



normal (Fig. 2, curve B). Whereas in the absence of silicic acid the curves show that the films break down at a pressure of about 15 dyne/cm. (Fig. 3, curve A), the films are now stable beyond 25 dyne/cm. Moreover, the change on compression, which in the absence of silicic acid is reversible, is no longer so. If the pressure is released and the film is then compressed a second time, there is no large increase in pressure until the area is reduced almost to 20 A^2/mean residue (Fig. 2, curve C).

These curves show that, although the silicic acid at this very low concentration interacts with the polyamide film, the properties of the film are unaltered until a critical pressure is reached. Then the adsorbed silicic acid units are pushed together close enough for chemical interaction (condensation or hydrogen bonding) to occur between them, and the film becomes coated by a continuous layer of polysilicic acid which need be no more than one unit thick. This is apparent from Fig. 3, where it is seen that the area at which the tanning occurs depends on the concentration of the silicic acid used.

In the experiments described, the films were compressed a few minutes after they had been spread. In other experiments, illustrated in Fig. 4, films were left on the silicic acid substrate for 48 or 60 hours before they were compressed. While the effect of tanning is not observed on solutions of polysilicic acid as dilute as 0·0001 M until the area of the polyamide film is reduced to about 25A^2/mean residue, it is observed over practically the whole range if the silicic acid is allowed to interact for a long period. This is not due to the silicic acid polymerizing in the substrate, because at this concentration silicic acid does not polymerize at all; on the contrary, it slowly depolymerizes. Even at a concentration of 0·005 M, it does not polymerize appreciably (Fig. 5). The silicic acid is slowly and irreversibly adsorbed to the protein layer, the two-dimensional concentration increasing until polymerization occurs beneath the film. The polyamide film thus acts as a collecting surface for the silicic acid. *In vivo* collagen may behave in the same way.

Here, then, is a mechanism by which a polysilicic acid layer may be built up from very dilute solutions of silicic acid and probably even from orthosilicic acid. It provides a feasible mechanism for the stabilization of collagen fibres in silicotic tissue. Whilst in the environment in which fibrosis is induced collagen may be the adsorbing phase, other suitable macromolecules might be equally effective in other biological systems.

The postulated mechanism of fibrogenesis is, then, that normally the response of the cell to certain

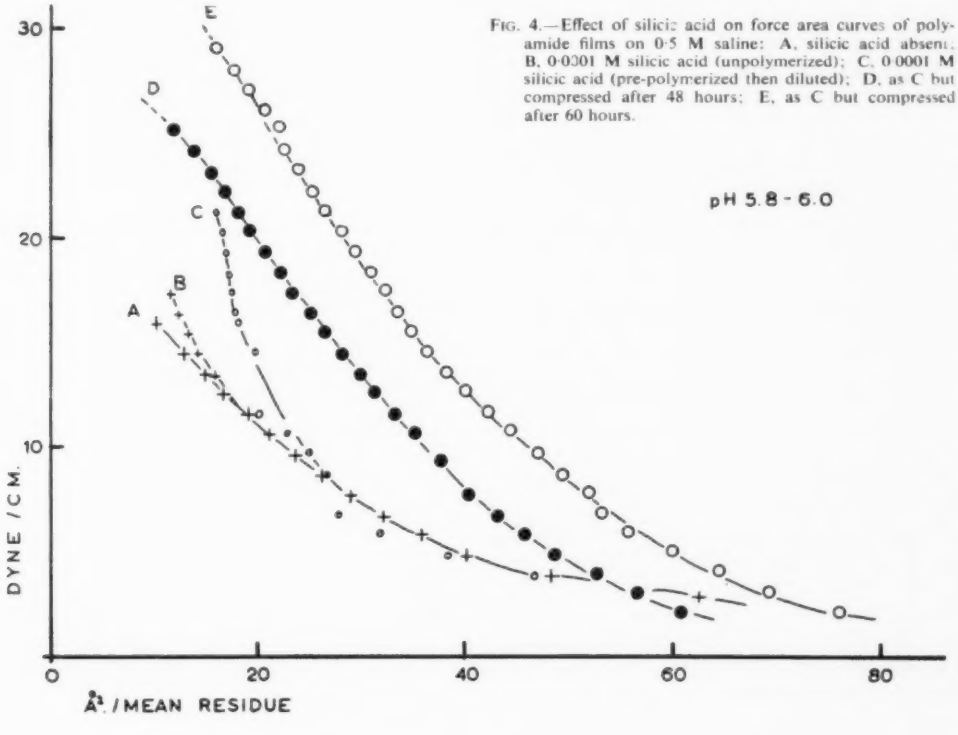


FIG. 4.—Effect of silicic acid on force area curves of polyamide films on 0·5 M saline: A, silicic acid absent; B, 0·0001 M silicic acid (unpolymerized); C, 0·0001 M silicic acid (pre-polymerized then diluted); D, as C but compressed after 48 hours; E, as C but compressed after 60 hours.

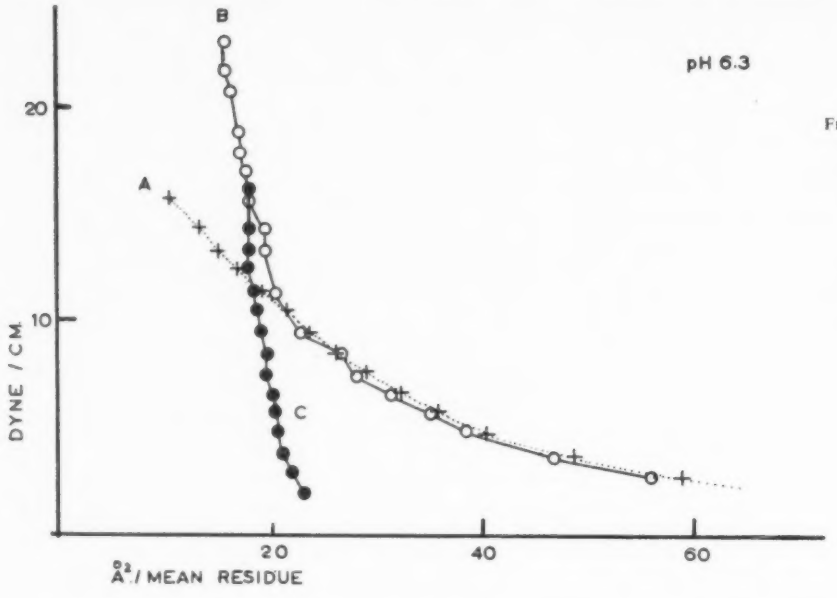
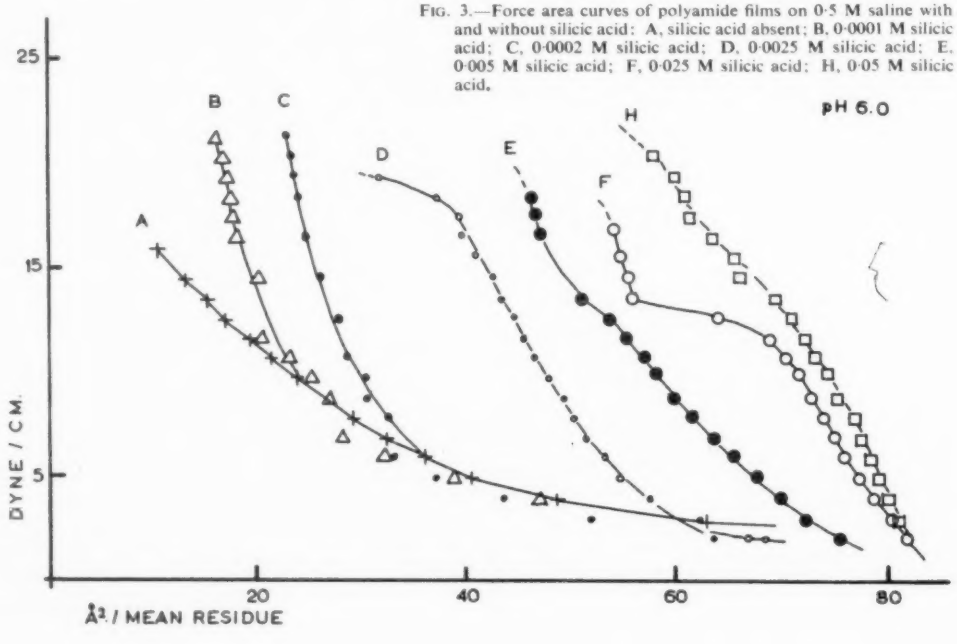


FIG. 2.—Force area curves of polyamide films: A, on 0·5 M saline; B, on 0·5 M saline + 0·0001 M silicic acid; C, same as B, second compression. The silicic acid is too dilute to affect the film until a pressure of 10 dyne/cm. is applied. The curve then rises steeply. Curve C shows that the protein-silicic acid complex is stable.

tion of say, 0·025 M, the form of the curve is altered. It rises steeply, and the change indicates that interaction has occurred and the film has been stabilized. Under these conditions the polysilicic acid particles which are adsorbed to the underside of the film approach one another so closely that interaction can occur between them, there is two-dimensional polymerization, and a permanent network forms. The film is said to be "tanned".

When the polyamide is spread on a solution of polysilicic acid diluted to 0·0001 M, the silicic acid apparently has no effect on the properties of the film at lower pressures, but above a force of about 10 dyne/cm., the curve rises steeply away from the

FIG. 3.—Force area curves of polyamide films on 0·5 M saline with and without silicic acid: A, silicic acid absent; B, 0·0001 M silicic acid; C, 0·0002 M silicic acid; D, 0·0025 M silicic acid; E, 0·005 M silicic acid; F, 0·025 M silicic acid; H, 0·05 M silicic acid.



normal (Fig. 2, curve B). Whereas in the absence of silicic acid the curves show that the films break down at a pressure of about 15 dyne/cm. (Fig. 3, curve A), the films are now stable beyond 25 dyne/cm. Moreover, the change on compression, which in the absence of silicic acid is reversible, is no longer so. If the pressure is released and the film is then compressed a second time, there is no large increase in pressure until the area is reduced almost to 20 A^2/mean residue (Fig. 2, curve C).

These curves show that, although the silicic acid at this very low concentration interacts with the polyamide film, the properties of the film are unaltered until a critical pressure is reached. Then the adsorbed silicic acid units are pushed together close enough for chemical interaction (condensation or hydrogen bonding) to occur between them, and the film becomes coated by a continuous layer of polysilicic acid which need be no more than one unit thick. This is apparent from Fig. 3, where it is seen that the area at which the tanning occurs depends on the concentration of the silicic acid used.

In the experiments described, the films were compressed a few minutes after they had been spread. In other experiments, illustrated in Fig. 4, films were left on the silicic acid substrate for 48 or 60 hours before they were compressed. While the effect of tanning is not observed on solutions of polysilicic acid as dilute as 0·0001 M until the area of the polyamide film is reduced to about 25A^2/mean residue, it is observed over practically the whole range if the silicic acid is allowed to interact for a long period. This is not due to the silicic acid polymerizing in the substrate, because at this concentration silicic acid does not polymerize at all; on the contrary, it slowly depolymerizes. Even at a concentration of 0·005 M, it does not polymerize appreciably (Fig. 5). The silicic acid is slowly and irreversibly adsorbed to the protein layer, the two-dimensional concentration increasing until polymerization occurs beneath the film. The polyamide film thus acts as a collecting surface for the silicic acid. *In vivo* collagen may behave in the same way.

Here, then, is a mechanism by which a polysilicic acid layer may be built up from very dilute solutions of silicic acid and probably even from orthosilicic acid. It provides a feasible mechanism for the stabilization of collagen fibres in silicotic tissue. Whilst in the environment in which fibrosis is induced collagen may be the adsorbing phase, other suitable macromolecules might be equally effective in other biological systems.

The postulated mechanism of fibrogenesis is, then, that normally the response of the cell to certain

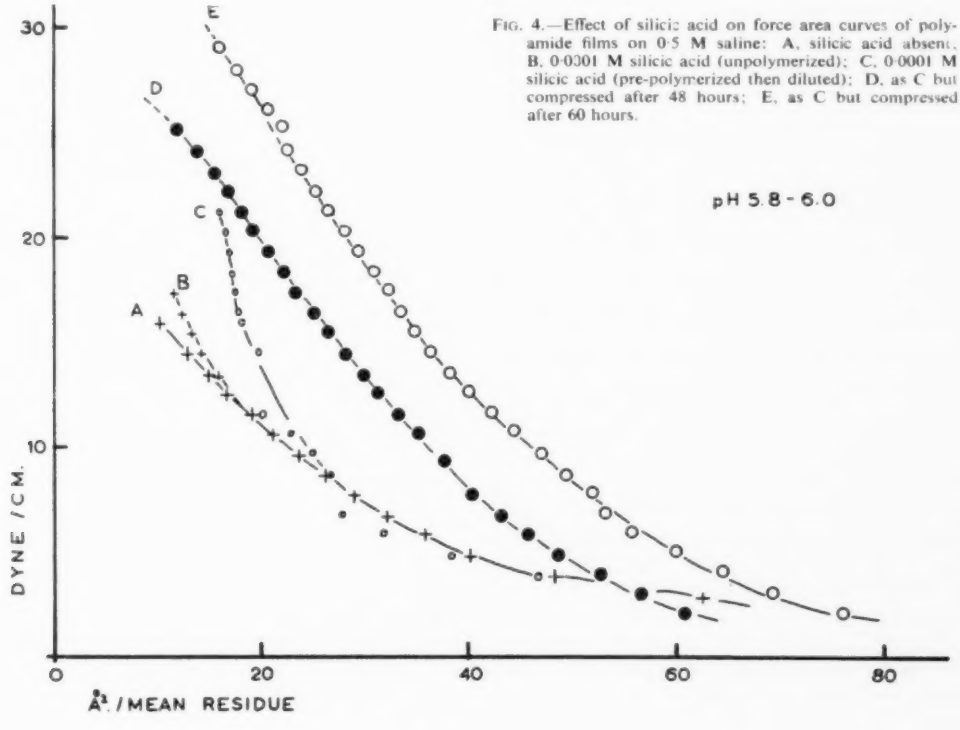


FIG. 4.—Effect of silicic acid on force area curves of polyamide films on 0·5 M saline: A, silicic acid absent; B, 0·0301 M silicic acid (unpolymerized); C, 0·0001 M silicic acid (pre-polymerized then diluted); D, as C but compressed after 48 hours; E, as C but compressed after 60 hours.

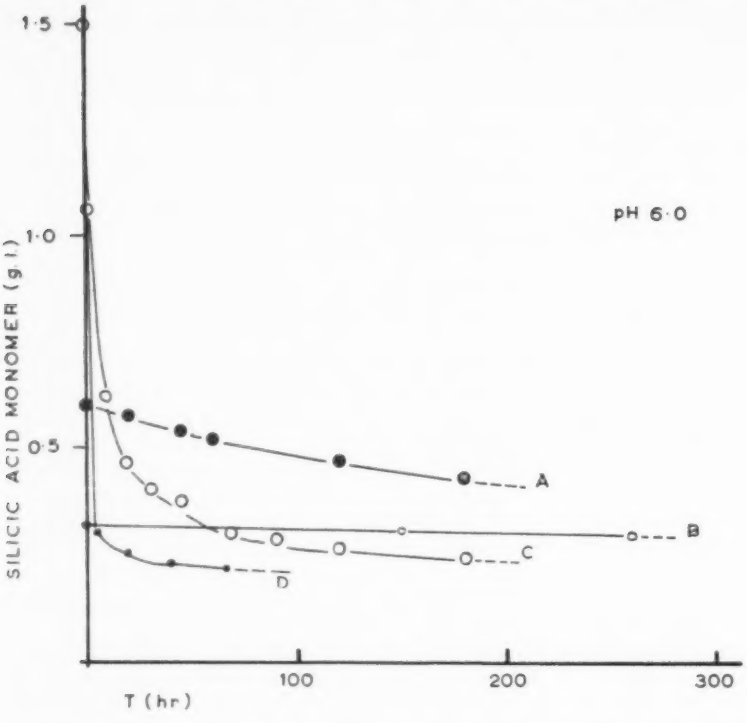


FIG. 5.—Rate of polymerization of silicic acid: variation with concentration. Polymerization is shown by a decrease in the concentration of monomer, measured as molybdate—reactive silicic acid. At 0·005 M no polymerization is apparent. Concentrations: A, 0·01 M; B, 0·035 M; C, 0·05 M; D, 0·1 M.

stimuli is the production of a collagen precursor in the form of very small units which are prevented from aggregating by the large amounts of polysaccharide which are secreted simultaneously. Most of the polysaccharide is later removed by polysaccharases, allowing the alignment of fibrils and the production of fibres with which a small amount of polysaccharide is associated as a cement substance. In normal fibrogenesis an equilibrium may be established, fibres being built up and others being simultaneously dispersed. When silicic acid is produced along with the collagen precursors, it is adsorbed irreversibly. Aggregation of the collagen chains is prevented by the polysaccharide which is produced by the cells at the same time, but once the complex has diffused away from the cells and the polysaccharide is hydrolised, the adsorbed silicic acid provides a cement substance which is permanent; there is no dispersion of the fibres.

This postulated mechanism is presented as a guide to future investigations. Considerable effort has been directed in some laboratories, following the introduction of the first extended solubility theory, towards the demonstration of the presence or absence of polysilicic acid in silicotic tissue. It must be apparent that there can be no justification for the expectation that silica gel or high polymers of the usual type occur in the tissues. The amount of silica available is too small, and if large quantities of high polymers were present, they could only retard fibrogenesis. The polymerization may only occur in two dimensions, along the protein fibres.

The authors are grateful to the British Steel Castings Research Association and to the British Rayon Research Association for financial assistance.

REFERENCES

Clark, S. G. (1955). Ph.D. Thesis, University of Reading.
——, and Holt, P. F. (1957). *Trans. Faraday Soc.*, **53**, 1509.
——, ——, and Went, C. W. (1957). *Ibid.*, **53**, 1500.
Cohen, S. S. (1942). *J. biol. Chem.*, **144**, 353.
Curran, R. C. (1952). *Brit. J. exp. Path.*, **33**, 82.
—— (1953). *J. Path. Bact.*, **66**, 271.
Einsele, W., and Grim., J. (1938). *Z. Bot.*, **32**, 545.
Fraser, R. D. B., and Macrae, T. P. (1959). *Nature (Lond.)*, **183**, 179.
Ginetzinsky, A. G. (1958). *Ibid.*, **182**, 1218.
Holt, P. F. (1957). *Pneumoconiosis*. Arnold, London.
——, and Bowcott, J. E. L. (1954). *Biochem. J.*, **57**, 471.
——, and Osborne, S. G. (1953a). *Nature (Lond.)*, **171**, 892.
——, ——, (1953b). *Brit. J. industr. Med.*, **10**, 152.
——, and Went, C. W. (1956). In *Symposium on Techniques in Polymer Science*. Royal Institute of Chemistry. Lectures, Monographs and Reports 1956, No. 5. London.
——, and Yates, D. M. (1954). *Brit. J. exp. Path.*, **35**, 52.
Jackson, D. S. (1953). *Biochem. J.*, **54**, 638.
—— (1954). *Ibid.*, **56**, 699.
Lund, J. W. G. (1950). *J. Ecol.*, **38**, 1.
Nageotte, J., and Guyon, L. (1935). *Arch. Sci. biol. (Napoli)*, **41**, 1.
Partridge, S. M. (1948). *Biochem. J.*, **43**, 387.
Sakabe, H., Hasegawa, T., and Yamada, K. (1956). *Bull. Inst. publ. Hth. (Tokyo)*, **5**, No. 2, p. 7.
Schwarz, W. (1957). In *Connective Tissue*. A Symposium organized by the Council for International Organizations of Medical Sciences, 1956, p. 144. Ed. R. E. Tunbridge. Blackwell Scientific Publications, Oxford.
Wheatley, K. (1957). *Research*, **10**, 76.

Brit. J. industr. Med., 1960, **17**, 31

CHANGES IN THE LUNG LIPIDS OF RABBITS AND GUINEA-PIGS EXPOSED TO THE INHALATION OF SILICA DUST

BY

G. S. MARKS* and L. W. MARASAS

From the Pneumoconiosis Research Unit of the South African Institute for Medical Research, Johannesburg, and the South African Council for Scientific and Industrial Research, Johannesburg, South Africa

(RECEIVED FOR PUBLICATION FEBRUARY 13, 1957)

Eight rabbits and 24 guinea-pigs were exposed to a silica dust cloud of about 40,000 pp./ml. (0·3-3·0 μ) and killed at four-weekly intervals up to 30 weeks. The guinea-pigs showed an increase of lung lipid and phospholipid; the latter showed a parallel with the rising collagen level estimated chemically. In the rabbits there was no increase of either lipid or phospholipid. The likely explanation is that the silica did not reach the lungs in sufficient quantity.

The findings of Gye and Purdy (1922) and Gye and Kettle (1922) that silicic acid and colloidal silica (forms of hydrated silica) are toxic to tissues gave rise to the solubility theory of silicosis according to which the silicic acid which is released from the silica particle is the agent causing fibrosis. Notwithstanding the large amount of experimental support for the solubility theory forthcoming from King and his co-workers from 1922 onwards, several facts cannot be explained by that theory, and King, Zaidi, and Nagelschmidt (1956) have suggested that the investigation of other theories might yield interesting information on the development of silicosis.

The possibility that lung lipids play a part in silicosis has been suspected for many years. Strachan and Simson (1930) noticed that one of the striking features in the well-formed silicotic nodule was the presence of lipid. According to these authors an increase of lipid is manifest as soon as silicotic fibrosis begins and increases with the advance of fibrosis.

Sabin (1932) made the important discovery that the phospholipid fraction of *Mycobacterium tuberculosis* was responsible for the formation of a lesion histologically similar to that found in tuberculosis, and both Gardner (1937) and Fallon (1937) were impressed by the similarity between silicotic and tubercular lesions. In order to explain the similarity between these two lesions Fallon (1937) postulated that after death of the phagocytic cell, resulting from interaction between silica and the cell, the intracellular material was released and it was the phospholipid portion of this intracellular material which produced a lesion similar in histological appearance to that produced by fractions of *Mycobacterium tuberculosis*.

In support of this postulate Fallon demonstrated a large increase in the phospholipid content of the lungs of rabbits after intratracheal injection of quartz dust and showed that intraperitoneal reinjection of the phospholipid recovered from these rabbit lungs caused lesions similar to those produced by the tubercular phosphatide of Sabin (1932).

The primary aim of this investigation was to confirm the large phospholipid increase observed by Fallon and to see if any correlation existed between the amount of phospholipid in the lung and the degree of fibrosis, as measured by the collagen content of the lungs (*cf.*, Stacy and King, 1954). In addition we were interested to obtain more detailed information on the changes in the lung lipids during the course of silica inhalation and for this reason analyses of lecithin and free and total cholesterol were carried out. We chose to analyse for these components of lung lipids since reliable methods are available for their direct determination. Finally analyses of the silica content of the lungs of the experimental animals were carried out to determine the amount of silica retained by each animal.

Method

Dusting.—Eight male rabbits and 24 female guinea-pigs were kept in cages in a room which was 1,000 cu. ft.

*Present address: Department of Botany, University of Chicago, Chicago 37, U.S.A.

in volume and exposed to the inhalation of silica dust. The dusting mechanism consisted of a cylinder of silica dust on a floating platform, the height of which could be varied by means of a water drip. The dust was removed from the cylinder by suction and injected into the room with compressed air.

The measurements of the dust cloud by means of a thermal precipitator were carried out by the Johannesburg Chamber of Mines Dust and Ventilation Laboratories, and some typical measurements of the concentration and size distribution of the dust are given in Table 1. The silica dust used was shown to contain

TABLE 1

DUST CONCENTRATION AND PARTICLE SIZE DISTRIBUTION OF SAMPLES OF SILICA DUST

Duration of Dusting (weeks)	Dust Concentration (particles/ml.)	Grading Percentages			
		> 2·2 μ	2·2-1·0 μ	1·0-0·3 μ	< 0·3 μ
5	47,376	9	18·4	29·6	43
7	50,400	3·7	17·6	33·6	45·1
18	60,280	1	18	39	42
19	69,700	1	24	35	40
20	21,920	3	16	36	45
22	25,400	1	3	27	69
23	22,300	1	3	29	67
25	25,200	1	9	45	45
26	60,120	2	21	34	43
28	36,153	2·2	9·2	36·8	51·8
29	41,360	3·9	14·3	38·7	43·1
30	20,380	2·5	16·2	36·3	45·0

98·6% SiO_2 by the colorimetric method of King *et al.* (1955) and 96% quartz by *x*-ray measurement.

Killing of Animals and Preparation of Lungs for Analysis.—One rabbit and two guinea-pigs were killed at approximately four-weekly intervals. In addition, one unexposed rabbit and one unexposed guinea-pig of similar weight to the exposed animals and having been kept on a similar diet were killed to act as controls. The animals were killed by striking them on the back of the neck with a metal bar and immediately cutting their throats. After exsanguination, their lungs were perfused with saline, removed, and dried between pieces of filter paper. The lungs were weighed and the apico-posterior segment of the left upper lobe and the apical segment of the left lower lobe were removed for histological examination. The remainder of the lungs was then weighed, chilled in an acetone-solid CO_2 mixture, and dried over phosphorus pentoxide *in vacuo*.

Silica and Collagen Analysis.—The dried lungs were weighed, ground up in a mortar, and approximately 200 mg. of dried powdered lung was removed for silica and collagen analysis. Silica was estimated by the colorimetric method of King, Stacy, Holt, Yates, and Pickles (1955), which is ideal for measurement of small quantities of silica and shown by the authors to be in good agreement with gravimetric methods. Collagen was determined by the method of Neuman and Logan (1950a and b) but included modifications suggested by Stacy and King (1954) and Martin and Axelrod (1953). The accuracy of this method has been shown by Neuman and Logan to be ± 5%.

Extraction and Purification of Lipid.—The residue of dried powdered lung was mixed with sea sand (Merck reagent), transferred to a "soxhlet" thimble, and extracted for eight hours with 150 ml. 3 : 1 alcohol-ether mixture and subsequently for eight hours with 100 ml. 2 : 1 chloroform-methanol mixture in a "soxhlet" apparatus. The alcohol-ether and chloroform-methanol extracts were combined and evaporated to dryness on a water-bath (60°) *in vacuo* (water-pump).

The residue was freed from non-lipid contaminants by the method of Folch, Lees, and Sloane-Stanley (1954), which has been shown to remove all non-lipid contaminants and less than 0·5% of lipids from the original extract. In accordance with this method the residue was dissolved in 30 ml. 2 : 1 chloroform-methanol mixture, 6 ml. of water added and the liquids mixed thoroughly. On standing, the system separated into two phases and the upper methanol-water phase containing all the non-lipid contaminants was removed with a pipette. The lower, predominantly chloroform phase containing all the lung lipids, was evaporated to dryness on a water-bath (60°) *in vacuo* (water-pump). The residue, which represented the total lipid, was dried over phosphorus pentoxide (*in vacuo*) overnight, and weighed. The total lipid fraction was dissolved in 15 ml. 2 : 1 chloroform-methanol mixture, and transferred quantitatively to a 25 ml. volumetric flask which was made up to volume with 2 : 1 chloform-methanol. All subsequent analyses were carried out in duplicate on aliquots of this solution.

Phospholipids.—Total lipid phosphorus was determined by the method of Fiske and Subbarow (1925) on a 1 ml. aliquot of solution and the phospholipid calculated on the basis of:—

Total phospholipid = total lipid phosphorus × 25.

The procedure adopted for the determination of lecithin was based on that of Hack (1947). It depends on the observation that lecithin and cephalin are completely hydrolysed by N-KOH in 18 hours at 37°, whereas under these conditions there is no hydrolysis of sphingomyelin. The choline in the hydrolysis mixture is a measure of the lecithin. For this determination a 5 ml. aliquot of the lipid solution was evaporated to dryness under reduced pressure at 60°. The residue was dissolved in 0·2 ml. of boiling ethanol and emulsified in 5 ml. of N-KOH by blowing the alkali vigorously from a pipette into the alcoholic lipid solution. The emulsion was kept at 37°C. for 24 hours and the amount of choline present after this period determined by the method of Glick (1944), as modified by Johnson, McNabb, and Rossiter (1948). This method has an accuracy of ± 3%. Colour density was measured in a Hilger Spekker absorptiometer using a green filter and a 4 cm. cuvette. A standard curve was constructed using solutions containing 1, 2, and 3 mg. of choline chloride. After a correction had been made for the dilution, the lecithin was calculated on the basis of:—

Lecithin = choline (as choline chloride) × 5·56.

Free and Total Cholesterol.—Free and total cholesterol were estimated in 1 ml. aliquots of the chloroform-methanol solution by a modification of the colorimetric method of Schoenheimer and Sperry (1934) incorporating improvements suggested by Sperry and Brand (1943) and

by Sobel and Mayer (1945). The method has an accuracy of ± 2%. Colour density was measured in a Hilger Spekker absorptiometer using a red filter.

Results and Discussion

Guinea-pigs.—The amounts and percentages (calculated on dry weight of lung) of silica and collagen in the lungs of experimental and control guinea-pigs, killed at different time intervals, are shown in Table 2. In accordance with expectation a steady rise in the silica content of the lungs with time was observed. The percentage silica in the lungs did not increase, however, due to the large increase in dry weight of the lungs with time. Therefore to express results as a percentage of dried lung is not appropriate, a fact that has been recognized already (*cf.*, Collins and Dible, 1935; Pratt, 1954).

The amounts of collagen in the lungs of the control guinea-pigs increased slowly with time due to the normal weight increases of the guinea-pigs. The amounts of collagen in the lungs of the experimental guinea-pigs were always somewhat larger than those in the controls.

Table 3 gives the weight of the guinea-pig at the beginning of the experiment, the weight when killed, the wet and dry weights of lungs, and the amount and percentage of lipid and phospholipid. The percentages are calculated on the basis of the dry, lipid, and silica-free lung. The wet and dry weights of the lungs of the guinea-pigs exposed to a minimum of 12 weeks of inhalation of silica were considerably greater than the controls. In these animals too an increase in lung lipid and phospholipid is apparent.

TABLE 2

AMOUNTS AND PERCENTAGES (CALCULATED ON DRY LUNG WEIGHT) OF SILICA AND COLLAGEN IN LUNGS OF EXPERIMENTAL AND CONTROL GUINEA-PIGS KILLED AT DIFFERENT INTERVALS

Description of Animal	Duration of Exposure (weeks)	Silica		Collagen	
		Total (mg.)	%	Total (mg.)	%
Control	0	—	—	30	4·3
Experimental	7	43	5·0	—	—
"	7	27	2·8	—	—
Control	0	0·8	0·1	—	—
Experimental	12	60	4·2	52	3·7
"	12	44	3·4	44	3·4
Control	0	2·0	0·25	38·5	4·6
Experimental	16	77	3·8	88·5	4·3
"	16	61	3·6	70	4·1
Control	0	—	—	46·4	5·2
Experimental	20	65	4·4	97	6·5
"	20	96	4·8	73	3·7
Control	0	—	—	50·5	4·3
Experimental	24	95	3·3	97·5	3·4
"	24	69	3·5	67·5	3·4
Control	0	—	—	56·5	5·4
Experimental	28	95	2·9	87·5	2·7
"	28	131	3·7	78·5	2·3
Control	0	—	—	61·0	5·6
Experimental	30	103	2·6	145	3·7
"	30	93	2·4	128	3·3
Control	0	—	—	70	7·0

These results with guinea-pigs are in accordance with Fallon's (1937) findings of an increase in phospholipid in the lungs of rabbits after intratracheal injections of silica. It is important to stress, however, that the large dry weight increase of the lungs in our experiments is not accounted for solely by the lipid increase.

In Table 4 are shown the amounts and percentages of lecithin and total and free cholesterol in the lungs of experimental and control animals killed at different time intervals (percentage calculated on dry,

TABLE 3

WEIGHTS OF EXPERIMENTAL AND CONTROL GUINEA-PIGS AND OF LUNGS AND AMOUNTS OF LIPID AND PHOSPHOLIPID IN LUNG

Description of Animal	Duration of Exposure (weeks)	Initial Weight of Animal (g.)	Final Weight of Animal (g.)	Wet Weight of Lung (g.)	Dry Weight of Lung (mg.)	Total Lipid		Phospholipid	
						Total (mg.)	%	Total (mg.)	%
Control	0	420	420	3·80	588	120	25·6	75	16
Experimental	4	410	440	3·35	645	133	26·0	99	19·3
Control	0	440	470	2·80	489	92	23·2	72	18·2
Experimental	7	490	660	4·5	865	181	28·2	101	15·8
"	7	440	630	5·05	957	244	35·6	193	28·1
Control	0	480	650	4·30	802	167	26·3	114	18·0
Experimental	12	470	750	6·63	1,422	334	32·6	224	21·8
"	12	500	680	6·67	1,280	294	31·2	208	22·0
Control	0	490	710	5·03	842	174	26·0	123	18·4
Experimental	16	440	790	8·90	2,040	653	49·9	376	28·6
"	16	400	820	9·55	1,710	453	37·9	228	19·1
Control	0	440	670	5·50	891	209	30·6	111	16·3
Experimental	20	390	750	7·42	1,495	272	23·6	126	10·9
"	20	460	780	9·83	2,000	407	27·3	224	15·0
Control	0	490	770	5·71	1,172	301	34·6	152	17·5
Experimental	24	550	880	13·37	2,910	683	32·0	384	18·1
"	24	420	800	9·00	1,975	427	28·9	213	14·4
Control	0	440	780	4·85	1,045	270	34·8	150	19·4
Experimental	28	420	730	13·61	3,280	892	39·0	616	26·9
"	28	500	1,070	14·38	3,510	1,217	56·0	816	37·7
Control	0	390	750	5·42	1,095	332	43·6	127	16·6
Experimental	30	520	1,080	20·83	3,950	1,350	54·0	847	33·9
"	30	450	780	17·61	3,860	1,001	36·2	606	22·0
Control	0	—	880	5·79	1,076	221	25·8	123	14·4

TABLE 4

AMOUNTS AND PERCENTAGES OF LECITHIN, TOTAL AND FREE CHOLESTEROL IN LUNGS OF EXPERIMENTAL AND CONTROL GUINEA-PIGS KILLED AT DIFFERENT INTERVALS

Description of Animal	Duration of Exposure (weeks)	Lecithin		Total Cholesterol		Free Cholesterol	
		Total (mg.)	%	Total (mg.)	%	Total (mg.)	%
Control	0	34	7·3	10·8	2·3	10·3	2·2
Experimental	4	40	7·8	15·2	3·0	14·3	2·8
Control	0	33	8·3	15·2	3·8	11·0	2·8
Experimental	7	30	4·7	17·5	2·7	11·0	1·7
"	7	59	8·6	22·4	3·3	19·2	2·8
Control	0	—	—	21·5	3·4	15·0	2·4
Experimental	12	98·5	9·6	30·5	3·0	26·0	2·5
"	12	66·0	7·0	25·4	2·7	21·8	2·3
Control	0	34·0	5·1	16·3	2·4	14·6	2·2
Experimental	16	195	14·9	37·0	2·8	34·0	2·6
"	16	108	9·1	28·4	2·4	25·3	2·1
Control	0	54	7·9	15·8	2·3	14·1	2·1
Experimental	20	50·6	4·4	20·5	1·8	14·7	1·3
"	20	88	5·9	36·0	2·4	28·0	1·9
Control	0	60	6·9	26·1	3·0	15·9	1·8
Experimental	24	194	9·1	50·0	2·4	37·8	1·8
"	24	92	6·2	33·3	2·3	23·2	1·6
Control	0	73	9·4	20·1	2·6	14·4	1·9
Experimental	28	357	15·5	57·6	2·5	51·3	2·2
"	28	429	19·9	70·6	3·3	56·1	2·6
Control	0	37	4·9	16·9	2·2	15·8	2·1
Experimental	30	530	21·2	71·0	2·8	68·4	2·7
"	30	342	12·3	70·0	2·5	60·0	2·2
Control	0	65·5	7·7	19·2	2·2	19·0	2·2

lipid, and silica-free lung). In all the animals submitted to a minimum of 12 weeks' exposure to silica dust there is a rise in the amount of each of these components in the lung lipids indicating that the large lipid increase in the lungs is due to an increase of all lipid components and not to any specific one.

Rabbits.—Table 5 gives the weights of rabbits at the beginning of the experiment, the weight when killed, wet and dry weights of lungs, and the amount and percentage of lipid and phospholipid. The percentages are calculated on the basis of dry, lipid, and silica-free lung.

In contrast to the results of Fallon (1937), it is apparent that there was no generalized increase in the content of lipid and phospholipid in the lungs of rabbits after inhalation of silica. The reason for this is probably that Fallon had used the technique of intratracheal injection whereby a massive dose of 250 mg. of silica was introduced into the lungs whereas with the inhalation technique used in our experiments the rabbits after 30 weeks' exposure to silica dust had still not inhaled 250 mg. of silica.

The difference between the results obtained with guinea-pigs and rabbits is of interest, since it has been noted in our laboratory for several years that by means of the inhalation technique it was very difficult to induce experimental silicosis in rabbits compared with guinea-pigs (Webster, unpublished work). In this respect the results assembled in Table 6, namely, the amounts and percentages (calculated on dry lung weight) of silica and collagen in the lungs of experimental and control guinea-pigs

TABLE 5

WEIGHTS OF EXPERIMENTAL AND CONTROL RABBITS AND OF LUNGS AND AMOUNTS OF LIPID AND PHOSPHOLIPID IN LUNG

Description of Animal	Duration of Exposure (weeks)	Initial Weight of Animal (g.)	Final Weight of Animal (g.)	Wet Weight of Lung (g.)	Dry Weight of Lung (g.)	Total Lipid		Phospholipid	
						Total (mg.)	%	Total (mg.)	%
Experimental	4	2,200	2,200	9·2	1·770	342	24·0	181	12·7
Control	0	1,800	1,900	8·1	1·47	281	23·6	152	12·8
Experimental	7	2,200	2,130	12·0	2·48	330	15·6	150	7·1
Control	0	1,800	1,840	7·95	1·49	268	21·9	145	11·9
Experimental	12	2,400	2,550	11·06	1·695	344	26·6	202	15·6
Control	0	2,100	2,470	9·47	1·50	346	30·0	236	20·4
Experimental	16	1,900	2,230	10·37	2·08	441	28·5	240	15·5
Control	0	2,300	2,300	9·92	1·82	411	29·2	205	14·5
Experimental	24	2,400	2,320	10·30	2·45	543	31·1	333	19·2
Control	0	2,200	2,580	7·71	1·52	334	28·2	140	11·8
Experimental	28	2,400	2,490	10·17	1·94	380	24·9	193	12·7
Control	0	2,200	2,550	8·48	1·96	373	23·5	190	12·0
Experimental	30	2,200	2,260	12·16	2·32	449	25·0	210	11·7
"	30	2,400	2,780	10·67	2·065	507	33·6	231	15·3
Control	0	2,400	2,750	8·77	1·960	458	30·5	167	11·1

TABLE 6

AMOUNTS AND PERCENTAGES (CALCULATED ON DRY LUNG WEIGHT) OF SILICA AND COLLAGEN IN LUNGS OF EXPERIMENTAL AND CONTROL RABBITS KILLED AT DIFFERENT INTERVALS

Description of Animal	Duration of Exposure (weeks)	Silica		Collagen	
		Total (mg.)	%	Total (mg.)	%
Experimental	4	—	—	—	—
Control	0	—	—	—	—
Experimental	7	34	1·4	—	—
Control	0	1	0·07	—	—
Experimental	12	52	3·1	72·5	4·3
Control	0	2·5	0·17	60	4·0
Experimental	16	89	4·3	135	6·5
Control	0	—	—	100·5	5·5
Experimental	24	169	6·9	95·2	3·9
Control	0	—	—	80·0	5·3
Experimental	28	33	1·7	82	4·2
Control	0	—	—	91	4·6
Experimental	30	72	3·1	125	5·4
"	30	46	2·2	112	5·4
Control	0	—	—	112	5·7

killed at different time intervals, are revealing. It is apparent that the rabbits have on the average inhaled approximately the same quantities of silica as the guinea-pigs (*cf.*, Table 2), and, since their lungs are larger than those of the guinea-pigs, it is to be expected that the rabbits would not be affected as severely as the guinea-pigs. The reason for the fact that the guinea-pigs and rabbits retained similar quantities of silica was not clear to us, and Dr. B. M. Wright (private communication) has kindly offered the following explanation :—

> "The most probable explanation for the difficulty of producing silicosis in rabbits is that under the usual laboratory conditions their activity, and therefore their respiratory minute volume, is low. According to Guyton (1947) the minute volume of guinea-pigs varies from about 100 to 350 ml./min. with an average of 150, whereas the respiratory minute volume of rabbits varies from about 270 to 1,200 ml./min. with an average of 800. Thus it would easily be possible for guinea-pigs, which are able to move about and be fairly active, to have a relatively greater respiratory rate taking into account the differences in lung volume. In support of this view is the observation that the weight of silica in the two species studied is about the same, namely, 75·6 mg. for guinea-pigs and 70·7 mg. for rabbits."

In Table 7 are shown the amounts and percentages of lecithin, total and free cholesterol (calculated on the dry, lipid, and silica-free weight of lung). No significant differences are to be noted between experimental and control animals.

This work was carried out in collaboration with Dr. J. C. Wagner, Senior Medical Officer of this Unit, to whom we are indebted for drawing our attention to the problem. We should like to express our gratitude to Mr. R. E. Silverton for carrying out the lung perfusions, and to Mr. Lawrie, of the Chamber of Mines Dust and Ventilation Laboratory, for the measurement of the concentration and size distribution of the dust. Finally we should like to thank Dr. I. Webster, Director of Pathology of this Unit, for many valuable suggestions during the course of this work.

TABLE 7

AMOUNTS AND PERCENTAGES OF LECITHIN, TOTAL AND FREE CHOLESTEROL IN LUNGS OF EXPERIMENTAL AND CONTROL RABBITS KILLED AT DIFFERENT INTERVALS

Description of Animal	Duration of Exposure (weeks)	Lecithin		Total Cholesterol		Free Cholesterol	
		Total (mg.)	%	Total (mg.)	%	Total (mg.)	%
Experimental	4	43·5	3·3	48	3·4	39·5	2·8
Control	0	39·2	3·3	42	5·5	33	2·8
Experimental	7	59	2·8	43	2·0	34·2	1·6
Control	0	41	3·3	44	3·6	26·8	2·2
Experimental	12	45	3·5	51	3·9	35·8	2·8
Control	0	48	4·2	42	3·6	30·4	2·6
Experimental	16	101	6·5	49	3·2	37·8	2·4
Control	0	68	4·8	46	3·0	41·5	2·7
Experimental	24	182	10·5	66	3·8	49·2	2·8
Control	0	50·3	4·2	44	3·8	32·0	2·7
Experimental	28	73	4·8	47·0	3·1	38·1	2·5
Control	0	65	4·1	39·3	2·5	37·1	2·3
Experimental	30	73	4·05	54·5	3·0	43·0	2·4
"	30	88·5	5·0	51·6	2·9	38·6	2·2
Control	0	64	4·3	44·5	3·0	35·0	2·3

REFERENCES

Collins, D. H., and Dible, J. H. (1935). *J. Hyg., (Camb.)*, **35**, 64.
Fallon, J. T. (1937). *Canad. med. Ass. J.*, **36**, 223.
Fiske, C. H., and Subbarow, Y. (1925). *J. biol. Chem.*, **66**, 375.
Folch, J., Lees, M., and Sloane-Stanley, G. H. (1954). *Fed. Proc.*, **13**, 209.
Gardner, L. U. (1937). *Amer. J. Path.*, **13**, 13.
Glick, D. (1944). *J. biol. Chem.*, **156**, 643.
Guyton, A. C. (1947). *Amer. J. Physiol.*, **150**, 70.
Gye, W. E., and Kettle, E. H. (1922). *Brit. J. exp. Path.*, **3**, 241.
——, and Purdy, W. J. (1922). *Ibid.*, **3**, 86.
Hack, M. H. (1947). *J. biol. Chem.*, **169**, 137.
Johnson, A. C., McNabb, A. R., and Rossiter, R. J. (1948). *Biochem. J.*, **43**, 573.
King, E. J., Zaidi, S. H., and Nagelschmidt, G. (1956). *A.M.A. Arch. industr. Hlth.*, **13**, 133.
——, Stacy, B. D., Holt, P. F., Yates, D. M., and Pickles, D. (1955). *Analyst*, **80**, 441.
Martin, C. J., and Axelrod, A. E. (1953). *Proc. Soc. exp. Biol. (N.Y.)*, **83**, 461.
Neuman, R. E., and Logan, M. A. (1950a). *J. biol. Chem.*, **184**, 299.
——, —— (1950b). *Ibid.*, **186**, 549.
Pratt, P. C. (1954). *Amer. J. Path.*, **30**, 1003.
Sabin, F. R. (1932). *Physiol. Rev.*, **12**, 141.
Schoenheimer, R., and Sperry, W. M. (1934). *J. biol. Chem.*, **106**, 745.
Sobel, A. E., and Mayer, A. M. (1945). *Ibid.*, **157**, 255.
Sperry, W. M., and Brand, F. C. (1943). *Ibid.*, **150**, 315.
Stacy, B. D., and King, E. J. (1954). *Brit. J. Industr. Med.*, **11**, 192.
Strachan, A. S., and Simson, F. W. (1930). Records of the International Conference held at Johannesburg, p. 231. International Labour Office, Geneva.

Brit J. industr. Med., 1960, **17**, 36.

DRUG TREATMENT OF EXPERIMENTAL SILICOSIS

BY

DINAH M. JAMES*, T. G. MORRIS, and J. MARKS†

From the Department of Pharmacology, Welsh National School of Medicine, the Pneumoconiosis Research Unit, Cardiff, and the Central Tuberculosis Laboratory, Cardiff

(RECEIVED FOR PUBLICATION FEBRUARY 12, 1959)

It has already been shown that tissue cultures of phagocytic cells may be protected against the toxic effect of silica dust by a number of organic bases and aluminium complexes. These compounds have now been used to treat mice after the administration of silica dust intravenously. Protective activity was measured by capacity to inhibit or retard the development of silicotic nodules in the livers of the experimental animals. Drugs active in this respect were an aluminium-dextran complex, phenazine B749, methylene blue, and compound 46-107. Compound 46-107 is related chemically to compound 48-80, the subject of a previous study of protective action, but lacks the latter drug's disruptive effect on mast cells.

The nature of the injury suffered by cells which ingest silica dust is not known. It is possible that the dust dissolves to give a toxic form of silicic acid but recent observations (*e.g.*, Englebrecht, Yoganathan, King, and Nagelschmidt, 1958) suggest that the biological activity of silica dust is a property of its surface, which presumably binds or distorts an important cell constituent.

Although there is experimental evidence that aluminium can protect animals against the effects of silica (Dworski, 1955), the value of aluminium in the prevention and treatment of silicosis in man is debatable (Kennedy, 1956), and it is uncertain whether the metal in the particulate form in which it is used can reach silica which has already entered lung tissue.

Previous observations on the interaction of methylene blue with silicic acid (James and Marks, 1956) suggested that soluble basic substances might be found with the capacity to neutralize the toxicity of silica dust. Subsequently an organic base, compound 48-80, was found to inhibit the development of silicosis in mice given silica dust intravenously (Marks, James, and Morris, 1958). The main pharmacological activity of compound 48-80, *i.e.*, disruption of mast cells and histamine release, would appear to preclude any practical advantage that might be gained from its action on silica. A more recent examination of related compounds, however, has shown that phagocytes may be protected *in vitro* against silica dust by drugs which do not show the mast cell effect (Marks, 1959). Several other substances were examined for protective activity in the same investigation.

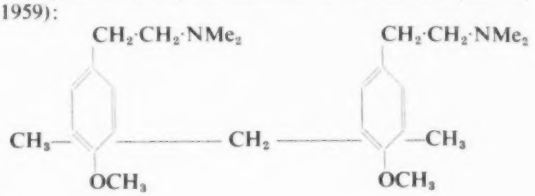
The present communication describes the treatment of mice, previously injected intravenously with silica dust, with a variety of drugs, which were selected chiefly on the basis of their ability to protect phagocytes *in vitro*.

Methods

Administration of Silica and Drugs.—Tridymite dust was given intravenously to male albino mice weighing about 20 g. in the manner described in our previous communication (Marks, *et al.*, 1958). In experiments 1 to 4, sample 4485 (Dvs = 1·4 μ) was used in a single dose of 3·5 mg. In experiment 5, sample 5145 (Dvs = 0·7 μ) was used in a dose of 5 mg. The dusts were provided by the Safety in Mines Research Establishment, Sheffield.

Except where otherwise stated, the drug schedules listed below all concern mice which had been given silica and received treatment by the intraperitoneal route beginning a few hours after the silica injection.

Compound 46-107.—This drug was prepared in two batches, (*a*) and (*b*), by the Wellcome Research Laboratories, New York; its formula is as follows (Marks, 1959):



*Present address: Department of Pharmacology, University College, Ibadan, Nigeria.

†Now at the Tuberculosis Reference Laboratory, Public Health Laboratory Service.

One dose was given daily, six days a week, using a fresh solution for each. The dose given initially was increased daily during the first week to reach the "normal dose" used thereafter throughout treatment.

In experiment 1, 11 mice were treated for 12 weeks with batch (*a*) in a normal dose of 0·5 mg. One mouse died in the first week and one in the ninth. Batch (*a*) was also used in experiment 2 but a higher dosage was attempted. However, unexpected deaths amongst the eight mice treated led to irregular schedules. Two mice out of three survived a course totalling 24 mg. in eight weeks, one of two mice survived 30 mg. in seven weeks, and one of three survived 36 mg. in seven weeks. The four survivors will be considered as a single group for which the mean normal dose was approximately 0·75 mg. and duration of treatment seven and a half weeks.

Batch (*b*) was used in experiment 3 in a normal dose of 0·5 mg. Treatment was stopped after six and a half weeks owing to a death in the fifth week and two deaths during each of the sixth and seventh weeks. On the last day of the seventh week two more mice died when the five survivors were sacrificed and all seven mice examined for silicosis.

In experiment 4, batch (*b*) was used at two dose levels. One group was given a normal dose of 0·4 mg. and all 13 mice in it died by the eighth week. A second group of 12 mice was given a normal dose of 0·25 mg. There was a death after one week, another after six weeks and two more mice died after seven weeks. The last of these was examined together with the survivors, which were sacrificed two days later. A third group of five mice was left untreated for four weeks and then given a normal dose of 0·25 mg. for six weeks (experiment 4c). None of this group died.

Aluminium Chelates.—Chelates of aluminium with oxytetracycline, sequestric acid, and dextran were prepared as described previously (Marks, 1959). The dextran (presented by Glaxo Laboratories Ltd.) was of the type used for restoring blood volume. In addition, Benger Laboratories Ltd. prepared for the present work a complex which contained 2·3% aluminium and 37·4% dextran of low molecular weight, together with water and NaCl. The latter dextran complex will be distinguished in the text by the letter B and the former by A.

The Al-dextran complex A used in experiment 1 contained 0·011% aluminium. It was given to seven mice intravenously in a dose of 0·2 ml. twice in the first week and 0·4 ml. twice in each of the second and third weeks. Subsequently 0·5 ml. was given intraperitoneally three times a week for nine weeks. A single death occurred in the tenth week.

For experiment 2, dextran complex A was prepared to contain 0·022% aluminium. It was given intraperitoneally to nine mice three times weekly, the dose being increased from 0·15 to 0·5 ml. over a period of two weeks and maintained at 0·5 ml. for a further five weeks. There were single deaths after two, three, and five weeks, and two animals died after seven weeks. The four survivors were left untreated for the eighth and ninth weeks. The same course of the complex was given to three control mice, which suffered no loss.

The Al-dextran complex A used in experiment 3 contained 0·011% aluminium and was given by the intraperitoneal route three times weekly, achieving a dose of 0·5 ml. in the first week, which was maintained for six more weeks. Twelve mice were treated, one dying in the sixth and another in the seventh week. Owing to an accident, control mice given similar treatment were lost. A group of four mice which had received no silica were therefore treated later (experiment 4b) with the same dosage of complex A. These controls were treated for 10 weeks, a duration intermediate between that of experiment 1 and experiment 3. (A full complement of controls was not practicable for experiment 1.)

Al-dextran complex B was used in a concentration equivalent to 0·037% aluminium and in a normal dose of 0·25 or 0·5 ml. given intraperitoneally three times weekly. The lower dose was achieved in steps over one week, the higher over two weeks. In experiment 2, nine mice were treated without loss using the lower dose for 12 weeks except for a rest period in the eighth and ninth weeks. A second group of nine were given the higher dose but, after three deaths in seven weeks, treatment was suspended for two weeks and the survivors were then killed. Three control mice were treated at each dose level. A normal dose of 0·25 ml. was used in experiment 3. The course was ended after seven weeks and the survivors killed following a death after three weeks and three deaths in the seventh week.

The complexes of aluminium with oxytetracycline and sequestric acid used in experiment 1 were prepared to contain 0·011% aluminium. Eleven mice were treated with the former and six with the latter. Both drugs were given intraperitoneally three times weekly in a dose of 0·2 ml. for the first week, 0·4 ml. for the next two weeks, and 0·5 ml. for the remaining nine weeks. An additional group of 11 mice (not reported in Table 1) were given the same dosage of the oxytetracycline complex intravenously but toxicity compelled a change to the intraperitoneal route after three weeks and discontinuance of treatment after two more weeks. There were three deaths and three more mice were killed because of skin lesions developing in the sacral and dorso-lumbar areas.

Phenazines.—Two compounds, B749 and B778, were chosen as the most active of a number provided by Dr. V. C. Barry for examination *in vitro* (Marks, 1959). These drugs were insoluble and suspensions were made in 10% dextran solution for intraperitoneal injection. In experiment 1, a dose of 1·6 mg. of compound B749 was given to seven mice three times weekly for six weeks. Only a single further dose was given in the following six weeks owing to signs of toxicity. There were deaths in the fifth, sixth, eighth, and ninth weeks. In experiment 2, 2·4 mg. of B749 was given once weekly for 12 weeks. Nine mice were treated, eight surviving. Compound B778 was used only in experiment 1; a dose of 1·6 mg. was given three times weekly for six weeks and, after two weeks' rest, for a further four weeks. One of the seven mice treated died in the seventh week.

Methylene Blue.—The dye was of the type supplied for vital staining. It was given intraperitoneally once daily for six days a week. Four groups, each of six mice, were

treated, three groups being given a dose of 0·2 mg. daily for two, four, and eight weeks respectively, and the fourth group a dose of 0·1 mg. daily for eight weeks. Four mice from each group were sacrificed after eight weeks and two after 12 weeks. However, there were two premature deaths in the former section and one in the latter, all in the high dose groups.

Other Substances.—A number of drugs which appeared to protect phagocytes against the toxic effect of silica *in vitro* were tested in a single experiment which will not be described in detail. The drugs, with their normal daily dose given in parenthesis, were as follows:—Stilbamidine isethionate (0·5 mg.), mepacrine methane sulphonate (0·5 mg.), chloroquine sulphate (0·5 mg.), promethazine hydrochloride (0·5 mg.), and compound 3349, a substituted methyl pyrimidine (1·0 mg.).

Readings

Examinations were confined to the liver. Approximately one-tenth of each was taken for histological examination. The following grades were used to classify the results, intermediate degrees being used in some instances:—

O = no structural abnormality
A = a few small collections of mononuclear cells (not more than were found in some normal mice)
B = a small to moderate number of early silicotic nodules with little collagen production
C = a large number of well-developed silicotic nodules, which were predominantly cellular although collagen was obvious
D = intermediate between C and E in that some lesions were mainly cellular and others mainly collagenous
E = a large number of nodules in which collagen predominated
F = a large number of nodules, almost entirely acellular

Collagen was estimated in the remainder of the liver by the method of Stacy and King (1954). The values

TABLE 1

DRUG TREATMENT OF EXPERIMENTAL SILICOSIS IN MICE

Experiment No. and Duration	Dose of Silica (mg.)	Treatment	Initial No. of Mice in Group	Examinations at End of Experiment	
				Total Liver Collagen (mg.)	Histological Gradings (see text)
1 (12 weeks)	3·5	Nil	14	16·0, 15·8, 13·3, 10·1, 10·0, 9·4, 9·3, 9·2, 7·9, 7·7, 7·4, 6·8, 6.6	E, E, C +, C, E, C, D +, C +, C, E, D +, D, D
	3·5	Compound 46-107 (medium dose)	11	5·7, 4·3, 3·9, 3·9, 3·8, 3·6, 3·3, 3·1, 2·4	B +, C, B, B, A +, B, A, B, B
	3·5	Al-dextran	7	9·1, 8·0, 6·1, 5·7, 5·3, 5·1	D +, C, B +, B, C, B
	3·5	Al-oxytetracycline	11	13·7, 12·0, 9·3, 8·8, 8·6, 7·9, 7·1, 6·8, 6·6, 5·8	D, E, D, C +, C +, D, C +, D, C, C
	3·5	Al-sequestric acid	7	11·0, 9·6, 9·3, 9·2, 7·9, 6·9	D, C +, D, D, D, D
	3·5	Phenazine B749 (6 weeks only)	7	6·1, 4·4, 4·3	C, B, A +
	3·5	Phenazine B778 (10 weeks only)	7	11·2, 10·1, 9·7, 9·6, 8·7, 7·2	E, D, D, D, D, D
	Nil	Nil	6	3·3, 3·0, 2·7, 2·7, 2·3, lost	O, A, A, O, O, O
	Nil	Compound 46-107 (medium dose)	3	3·3, 3·2, 3·0	A, O, O
	Nil	Al-oxytetracycline	6	3·6, 3·2, 3·0, 2·8, 2·3	O, A, A, O, O
2a (9 weeks)	3·5	Nil	8	12·6, 9·2, 8·2, 8·1, 7·6 7·0, 6·4	D, C +, D, C +, C +, D, C
	3·5	Compound 46-107 (high dose)	8	3·9, 3·2, 3·2, 3·1	A, B, A +, A +
	3·5	Al-dextran (high dose, 7 weeks)	9	6·9, 5·6, 4·7, 4·1	C, A +, A +, B +
	3·5	Al-low molecular weight dextran (high dose, 7 weeks)	9	11·0, 5·1, 4·8, 4·8, 3·0, lost	D, D, C +, C +, C +, D
	Nil	Al-dextran (high dose)	3	6·1, 4·8, 3·8	B +, B, A +
	Nil	Al-low molecular weight dextran (high dose)	3	3·9, 3·3, lost	B, B, B
2b (12 weeks)	3·5	Nil	8	17·4, 15·1, 11·3, 10·9, 9·1, (3·9, 1·9*)	C +, D, E, D, D, (C +, C)
	3·5	Al-low molecular weight dextran (10 weeks only)	9	10·8, 10·3, 9·8, 9·3, 9·2, 8·9, 7·0, 6·6, 4·7	E, D, C, D +, D, D +, C +, D, C +
	3·5	Phenazine B749 (low dose)	9	5·9, 5·2, 5·1, 4·9, 4·9, 4·0, 4·0, 3·9	C +, B, C, C, B +, B, B, B
	Nil	Al-low molecular weight dextran (10 weeks only)	3	3·8, 3·7, 3·6	B, B, B
3 (7 weeks)	3·5	Nil	20	10·3, 9·9, 9·8, 9·0, 7·6, 7·1, 7·0, 7·0, 6·9, 6·4, 5·7, 5·7, 5·4, 4·9, 4·7	D, C +, C +, C +, C +, C +, C +, C, C, C +, C, C, C, C, C
	3·5	Compound 46-107 (medium dose)	12	4·1, 3·8, 3·4, 3·3, 3·0, 3·0, lost	A +, A +, A +, A +, A +, O, A +
	3·5	Al-dextran	12	4·6, 4·0, 3·9, 3·9, 3·8, 3·8, 3·7, 3·4, 3·3, 2·9	B, B, B, A +, A +, A +, B, A +, B, A +
	3·5	Al-low molecular weight dextran	11	9·4, 8·4, 6·3, 6·1, 5·4, 4·9, 4·9	C +, D, C, C +, C, D, C
4a (7 weeks)	3·5	Nil	7	9·0, 7·1, 6·3, 6·2, 5·9, 4·6	D, C +, D, C, C +, D
	3·5	Compound 46-107 (low dose)	12	3·9, 3·9, 3·6, 3·4, 3·2, 2·8, 2·8, 2·6, 1·9	C, B +, D, C, C +, B +, B, B, B
4b (10 weeks)	Nil	Al-dextran	4	3·7, 3·4, 3·1, 2·7	A +, A +, A +, A +
5b† (12 weeks)	5	Nil	4	7·4, 6·1, 5·7, 3·4	D +, D, D +, B
	5	Methylene blue (2 weeks only)	2	5·0, 2·4	C, O
	5	Methylene blue (4 or 8 weeks only)	6	2·8, 2·7, 2·6, 2·5, 2·3	O, O, A, B, O
	Nil	Nil	4	2·6, 2·3, 2·2, 1·9	A, O, O, O

*These two values are attributed to a technical fault.
†See text for an account of 5a.

presented in Table 1 are corrected for the portion of liver taken for histology and are given in the same order as the histological gradings.

Results

Compound 46-107.—With the higher dosages deaths became frequent after several weeks' treatment. More occurred with batch (*b*) than with (*a*) but, as the two samples were not used simultaneously, variation in the susceptibility of the mice cannot be excluded. Details of the mortality are given above. The drug afforded a considerable degree of protection against the development of silicosis in experiments, 1, 2a, and 3. Protection was less but still obvious in experiment 4a where the dose was reduced to 0·25 mg. daily.

The result of experiment 4c, in which treatment was started four weeks after the silica injection, has been omitted from Table 1 because of certain special histological features. The controls given silica but left untreated had liver collagen values of 10·6, 9·4, 9·2, 7·1, and 6·6 mg., and histological gradings of D+, D+, D, E, and D respectively. The mice receiving delayed treatment had collagen values of 5·6, 5·3, 4·1, and 4·1 mg., the fifth estimation being lost. Histologically, the livers of this group of treated mice were difficult to classify in the grades used for the other experiments. Their lesions tended to be stellate and were less cellular than in the untreated mice, giving the impression that although existing damage had not been repaired, progression of the disease had been halted or slowed. It should be noted that a dose of only 0·25 mg. was used in this experiment.

Statistical analysis of the liver collagen values for mice given silica and subsequently treated with compound 46-107 shows them to have been significantly lower than the values for untreated silicotic mice. The level of significance was $P < 0.01$ in each of the five experiments 1, 2a, 3, 4a, and 4c.

Aluminium Chelates.—The complex of aluminium with ordinary dextran (molecular weight 150,000) clearly protected mice against silicosis but not as well as 46-107. A dose equivalent to 55μg. aluminium (three times weekly intraperitoneally) was well tolerated but double this amount proved toxic. In the livers of both normal and silicotic mice treated with either dose small aggregations of cells were seen with abundant rather hyaline cytoplasm which were associated with a minor degree of collagen production. These cells, which were assumed to be altered macrophages or reticulo-endothelial cells, were not seen in mice that received dextran in association with phenazine compounds.

The complex with dextran of low molecular weight had very little protective action. It induced liver changes similar to those described immediately above. The oxytetracycline and sequestric acid chelates of aluminium had no protective action.

Statistical analysis of the liver collagen values in mice given silica and treated with aluminium complexes and those left untreated gives the following levels of significance for the differences observed:—

Experiment 1		
Al-dextran	$0.05 > P > 0.02$	(significant)
Al-oxytetracycline	$0.3 > P > 0.2$	(not significant)
Al-sequestric acid	$0.5 > P > 0.4$	(not significant)
Experiment 2a		
Al-dextran (high dose)	$0.05 > P > 0.02$	(significant)
Al-low molecular weight dextran (high dose)	$0.1 > P > 0.05$	(not significant)
Experiment 2b		
Al-low molecular weight dextran	$0.5 > P > 0.4$	(not significant)
Ditto, omitting aberrant controls	$0.02 > P > 0.01$	(significant)
Experiment 3		
Al-dextran	$P < 0.01$	(significant)
Al-low molecular weight dextran	$0.5 > P > 0.4$	(not significant)

Phenazines.—A considerable degree of protection against the development of silicosis was afforded by the phenazine compound B749 in both experiments 1 and 2b. However, the dose chosen for the first experiment was too high and four of the seven treated mice died. Phenazine compound B778 was well tolerated but not protective.

The levels of significance for collagen values in the phenazine experiments are as follows:—

Experiment 1		
Phenazine B749	$0.02 > P > 0.01$	(significant)
Phenazine B778	$0.7 > P > 0.6$	(not significant)
Experiment 2b		
Phenazine B749	$0.05 > P > 0.02$	(significant)
Ditto, omitting aberrant controls	$P < 0.01$	(significant)

Methylene Blue.—The dust suspension used in experiment 5 was unsatisfactory and the degree of silicosis in the untreated mice killed at eight weeks was too low for useful comparisons to be made. However, in the second part of the experiment, terminated four weeks later, the results did allow the effect of treatment to be assessed. As the number of mice observed for 12 weeks was small, those which received the higher dose of dye for four and eight weeks and the lower dose for eight weeks have been grouped together. A considerable degree of protection by the dye was evident in this group, the liver collagen values being significantly lower than in the untreated mice ($P < 0.01$).

Other Drugs.—The experiment to determine the protective effects of stilbamidine, mepacrine, chloroquine, promethazine, and compound 3349 was technically satisfactory but no inhibitory action on the development of silicosis was demonstrated histologically. Collagen estimations were therefore omitted and the results will not be reported in detail.

Discussion

In evaluating the antagonists to silica, which were the subject of the present investigation, account must be taken of the relatively large dose of highly fibrogenic dust (tridymite) against which protection was sought. None of the drugs studied gave complete protection but several gave results which indicated that the drug treatment of silicosis in man is a reasonable target.

Experiments *in vitro* suggested that compound 46-107, although somewhat more toxic to isolated cells, was a more potent antagonist to silica than compound 48-80, the first of the series to be examined. It was therefore disappointing in the present investigation to find that the dose of 46-107 had to be raised to a toxic level to achieve results comparable with those reported for 48-80. Although 46-107 lacks the disruptive effect of 48-80 on mast cells (Norton, 1958), it was not possible to treat mice with a dose very much larger than that previously used for 48-80 (Marks, *et al.*, 1958). However, it now appears possible that toxicity to mast cells and protection against silica may be dissociated in this group of drugs, encouraging the hope that effective but less toxic derivatives may be found.

In previous experimental work and in clinical practice, aluminium has been used in a relatively insoluble form. The soluble preparations of aluminium described in the present work were devised to see whether systemic treatment was practicable and effective. There was little difference *in vitro* between the protective activities of the chelates with oxytetracycline, sequestric acid, or normal dextran (Marks, 1959), and it is not clear why the first two were ineffective in mice. The chelate with dextran of low molecular weight had little activity either *in vitro* or *in vivo*. As both types of dextran chelate produced small lesions in the livers of normal mice, the use of such soluble aluminium complexes must be considered to carry a hazard until their effect in other species has been studied. There may be circumstances, however, such as in the treatment of silico-tuberculosis, in which side-effects might be risked for a temporary abatement of the silicotic element while the infective process is treated.

Phenazines have been studied and found effective by Barry and Conalty (1958) in connexion with the chemotherapy of experimental tuberculosis. Several of the group have been found to protect phagocytes against the effect of silica *in vitro*, although there was doubt as to the specificity of their action (Marks, 1959). Compounds B749 and B778 were both particularly active *in vitro* but in the present study only the former protected mice against the effects of silica. The difference appears to have been due to a lack of diffusibility in the case of B778, which may also account for its low toxicity. It would be premature to discuss the potentialities of compound B749 but a drug which may protect against both silica and tubercle bacilli is of obvious interest.

The use of methylene blue as an antagonist to silica was suggested by an earlier observation that it flocculates with polysilicic acid (James and Marks, 1956). As the dye is highly toxic for isolated macrophages, tests *in vitro* were unsatisfactory. Protection *in vivo* was clearly seen in the single experiment made on mice but circumstances have prevented the institution of the further animal tests which are obviously desirable.

It must be admitted that the dosage of the protective drugs described has been pushed to the point of toxicity in order to demonstrate unequivocal evidence of their activity. It is therefore highly probable that if less silica had been administered, more tolerable drug régimes could have been used with benefit. However, since the relative toxicity and protective power of a drug in one species may well be quite different in another, studies on mice such as the present one can claim to do no more than indicate lines of research of potential value.

We are indebted to Dr. V. C. Barry, the Wellcome Research Laboratories, New York, Benger Laboratories Ltd., and Glaxo Laboratories Ltd., for gifts of drugs acknowledged in the text, and to the Medical Research Council for a grant for apparatus. Our thanks are due also to Mr. C. A. Lediard for preparing the histological material, to Dr. G. Nagelschmidt for providing silica dusts, and to Dr. E. Lewis-Faning for the statistical analyses.

References

Barry, V. C., and Conalty, M. L. (1958). *Amer. Rev. Tuberc.*, **78**, 62.
Dworski, M. (1955). *A.M.A. Arch. industr. Hlth*, **12**, 229.
Englebrecht, F. M., Yoganathan, M., King, E. J., and Nagelschmidt, G. (1958). *Ibid.*, **17**, 287.
James, Dinah, M., and Marks, J. (1956). *J. Hyg. (Lond.)*, **54**, 342.
Kennedy, M. C. S. (1956). *Brit. J. industr. Med.*, **13**, 85.
Marks, J. (1959). *Ibid.*, **16**, 166.
——, James, Dinah M., and Morris, T. G. (1958). *Ibid.*, **15**, 1.
Norton, S. (1958). Personal communication.
Stacy, B. D., and King, E. J. (1954). *Brit. J. industr. Med.*, **11**, 192.

Brit. J. industr. Med., 1960, **17**, 41.

A COMPARISON OF THE EMOTIONAL STABILITY OF COAL-MINERS AND RAILWAYMEN

BY

JUDITH S. LION

From the Nuffield Department of Industrial Health (University of Durham), King's College, Newcastle upon Tyne

(RECEIVED FOR PUBLICATION FEBRUARY 2, 1959)

A comparison has been made of the emotional stability of coal-miners with that of railwaymen. Sixty-seven miners and 50 railwaymen were given a small battery of objective tests of emotional instability. A clinical group of 17 psychiatric patients diagnosed as emotionally unstable was also tested.

Tests of significance were carried out comparing the scores of the miners with those of the railwaymen and the railwaymen with the clinical group. In addition a factor analysis was made of the scores of the miners.

A comparison of the miners and railwaymen on Heron's test of emotional instability revealed a significant difference, the miners scoring more emotionally unstable scores than the railwaymen. The remaining tests, with the exception of those for fluency and hand persistence, failed to discriminate between these two groups.

Heron's test (both parts) was also the only one to reveal significant differences between the clinical group and the railwaymen. These were in the expected direction.

The results on Heron's test suggest that miners are less stable than railway workers and this is attributed to the environmental stresses of mining. It is suggested that many tests purporting to measure emotional instability are too sensitive to other personality variables.

This paper describes a study made to determine whether coal-miners are more emotionally unstable than workers in another industry. It formed part of a larger investigation into the emotional stability of miners, in which the present author was able to show (Lion, 1958) that miners suffering from nystagmus were more unstable than miners without the disease. It has been suggested (Heron and Braithwaite, 1953) that coal-miners who work underground are not as stable as those employed above ground. In this research, a group of miners and a group of railway workers were compared on a small battery of objective tests of emotional instability to see whether there was any significant difference between them.

Method

The Miners.—Sixty-seven men were selected at random. Their mean age was 55 years and they were all coalface workers, having spent an average of 30 years at the coalface. This group will be referred to as "the miners". Further details of their selection are given in the paper on the initial study of nystagmus (Lion, 1958).

The Railwaymen.—These men, selected from the same area, were employed in a variety of jobs ranging from engine drivers to porters. Their mean age was 52 years and none of them had ever worked in the mines. They were attending routine biennial medical examinations and the first 50 men to attend, in the appropriate age group, were selected.

The Tests

Heron 1 (1956): A Two-Part Personality Inventory.—This two-part personality measure consists of 110 statements which can be answered as "true" or "not true" self descriptions by the subjects. The first part, 74 items, contains 20 items which are used as the basis for a score of emotional maladjustment. Most of the remaining items are buffers which cause the section as a whole to appear as a "health inventory".

In the original validation, the test was given to more than 1,600 people and "has been used widely under various conditions in industry and elsewhere" (Heron, 1956). This test had a misclassification rate of only 13% when given to Heron's original sample of "normals" and neurotic patients in hospital.

Heron 2.—The second part of the measure consists o f 36 items, 12 of which are used as the basis for a score of sociability (Heron, 1956).

Annoyances (Bennett, 1945).—This test records the

number of items which the subject records as annoying him from a list of 60 possible annoyances.

Food Aversions (Wallen, 1945).—This is the number of aversions recorded from a list of 24 items of food.

Hand Persistence (Eysenck, 1947).—The number of seconds the subject can maintain his grip on a hand dynamometer at two-thirds of his maximum grip.

Fluency (Eysenck, 1947).—The number of "round" objects a subject can name in one minute.

Leg Persistence (Eysenck, 1947).—The number of seconds the subject can hold his right leg fully extended at a given distance above a chair.

All of these tests except Heron 2 have been shown to discriminate between "normals" and "neurotics'. Heron 2 is a test of sociability but not of emotional instability.

Results

Comparison of Groups.—The histogram (Fig. 1) demonstrates the difference between the two groups on Heron 1 showing the higher percentage of railway workers at the low scores and the greater percentage of miners at the high scores. Heron considers scores of 0 to 7 as "probably well adjusted", scores of 8 and 9 as "doubtful", and scores over 10 as "probably maladjusted".

Table 1 shows the mean scores for both groups on the seven tests with the appropriate levels of significance for differences between the groups.

On Heron 1, the main test of emotional instability, Student's t test showed the difference between the two groups to be significant ($P < 0.01$). On the hand persistence test the miners scored significantly higher ($P < 0.01$) than the railway workers, *i.e.*, they showed greater persistence. The fluency test discriminated between the two groups at the 0.02 level of significance, the miners obtaining lower (more neurotic) scores than the railwaymen.

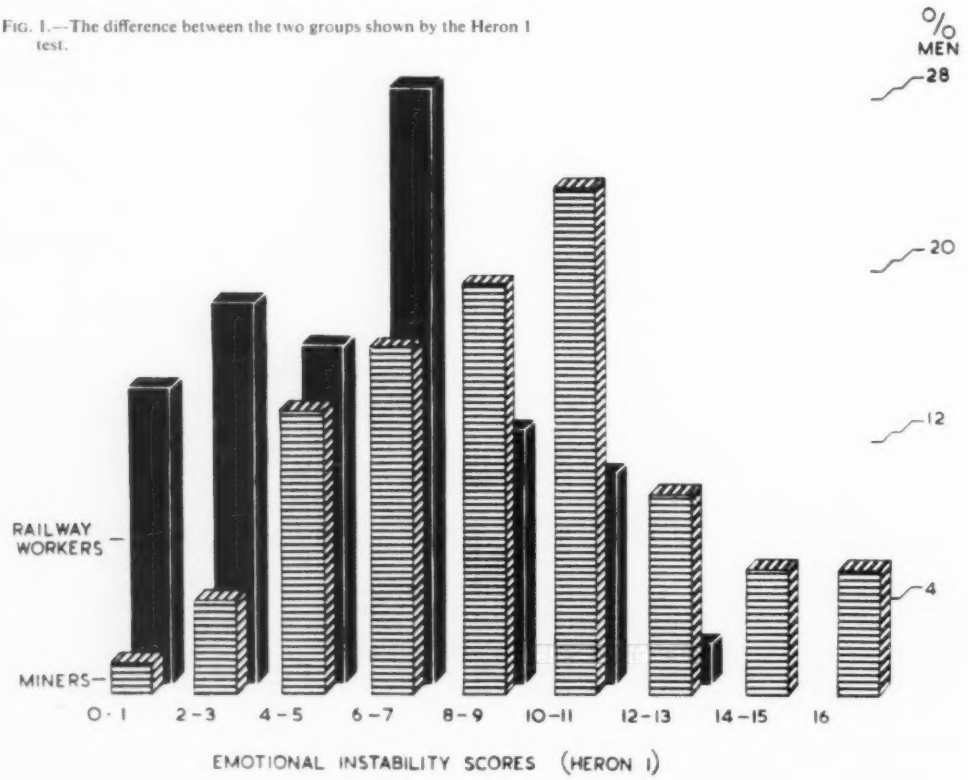
The results on Heron 1 (see Table 1) suggest that

TABLE 1
MEAN SCORES AND LEVELS OF SIGNIFICANCE

Tests	Mean Scores		t	P
	Railway Workers (N = 50)	Miners (N = 67)		
Heron 1 (emotional instability)	6·00	8·12	3·20	0·01
Heron 2 (unsociability)	5·32	5·91	1·22	ns
Annoyances	38·68	37·08	0·65	ns
Food aversions	3·98	4·51	0·87	ns
Hand persistence	43·88	57·49	2·76	0·01
Fluency	8·64	7·18	2·48	0.02
Leg persistence	54·16	60·36	0·66	ns

ns = not significant.

FIG. 1.—The difference between the two groups shown by the Heron 1 test.



miners are more unstable than railway workers. However, the author felt that this test over-emphasized undue preoccupation with health. Six of the 20 items scored in the test seemed to be concerned solely with this, and it was felt that the significant difference obtained between the two groups might be due to the miners being more pre-occupied with their health rather than to any difference in emotional stability. This is of the utmost importance as miners, because of the very nature of their work, might justifiably worry more about their health than others who work in a less dangerous occupation. These six items were:—

No. 5 I am troubled by sick headaches.
23 My eyesight is sometimes blurred.
33 My bowels are not opened every day.
44 My physique is excellent.
55 I have no particular physical or health problems.
69 I catch cold frequently.

In order to overcome this possible bias the score of each man in both groups was re-calculated omitting these six items. In fact, this recalculation produced a greater difference between the two groups, t being 4·09 ($P < 0·001$). A possible explanation of this may be that owing to the rigorous nature of their life miners are less concerned with trivial complaints.

An attempt was later made to validate the battery by testing 17 out-patients of a psychiatric clinic, all diagnosed by a psychiatrist as being neurotic. The small number in the group was due to the great difficulty in obtaining subjects, but it was considered large enough to compare their scores with those of the railwaymen.

Student's t test revealed significant differences between the two groups on Heron 1 ($P < 0·001$) and on Heron 2 ($P < 0·05$). These differences were in the expected direction; the annoyances test discriminated in the opposite direction from that expected, *i.e.*, the railwaymen obtained significantly higher scores ($P < 0·02$) than the neurotic group. The remaining tests revealed no significant differences between the two groups.

Factor Analysis.—The scores of the 67 miners were intercorrelated (Table 2) and the matrix factor analysed using the centroid method with three iterations. After the third iteration the obtained communalities did not differ from those used as estimates in the last iteration by more than $\pm$ 0·02.

Three factors were extracted, accounting for 32·6% of the variance. Two rotations were carried out. The criteria employed in rotating were: (1) to maximize the number of zero or near zero loadings; (2) to seek a positive manifold.

The rotations were as follows:—

f_2 with f_3 at 35° giving F_2' and F_3'
f_1 with f_3 at 45° giving F_1' and F_3''

Table 3 shows the factor loadings and communalities of each test on the three factors before and after rotation and the direction in which the tests were scored.

Fig. 2 shows the final position of the tests on factors 1 and 3. The most probable interpretation

TABLE 2
INTERCORRELATION MATRIX

Test	Scoring Direction	1	2	3	4	5	6
Heron 1 (emotional instability)	Many						
Heron 2 (unsociability)	Many	0·107					
Annoyances	Many	0·088	−0·104				
Food aversions	Many	0·158	0·256	−0·127			
Hand persistence	Low	0·153	0·160	−0·007	−0·193		
Fluency	Few	0·097	0·190	0·008	0·127	0·022	
Leg persistence	Low	0·267	0·190	0·101	−0·064	0·412	0·063

TABLE 3
FACTOR LOADINGS AND COMMUNALITIES OF EACH TEST BEFORE AND AFTER ROTATION

No.	Tests	Scoring Direction	Unrotated				Rotated			
			f_1	f_2	f_3	h^2	F_1	F_2	F_3	h^2
1	Heron 1 (emotional instability)	Many	0·40	−0·18	0·33	0·30	0·55	0·04	−0·02	0·30
2	Heron 2 (unsociability)	Many	0·58	0·27	−0·19	0·44	0·19	0·12	−0·63	0·44
3	Annoyances	Many	−0·06	−0·24	0·21	0·11	0·18	−0·08	0·26	0·11
4	Food aversions	Many	0·33	0·49	0·27	0·42	0·19	0·56	−0·27	0·42
5	Hand persistence	Low	0·42	−0·46	−0·32	0·50	0·30	−0·57	−0·30	0·50
6	Fluency	Few	0·23	0·13	0·08	0·08	0·16	0·15	−0·17	0·08
7	Leg persistence	Low	0·48	−0·45	−0·04	0·43	0·50	−0·39	−0·18	0·43

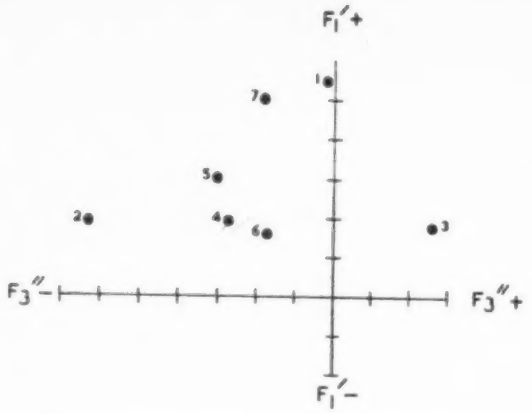


FIG. 2.—Relation between F_1 and F_3 after final rotation.

of these factors appears to be as follows:—

F_1 = Emotional instability
F_2 = Possibly a factor of persistence
F_3 = Unsociability

Discussion

The first suggestion that miners are less stable than others came from Halliday (1943) who held that miners applying for sickness benefit were more neurotic than other workers who applied. Heron and Braithwaite (1953) have since provided evidence that miners working at the coal-face are more neurotic than those employed above ground.

There is certainly much evidence to suggest that miners work in an environment which may be especially conducive to the development of neurosis. Despite the enormous improvements in safety during recent years there are still many accidents, and even in 1956 the total number of men killed in pit accidents in Great Britain was as great as 330 (Ministry of Power Statistical Digest, 1956). A large number of the miners in the present series had been involved in some minor accident, and it was not uncommon for a man to have one or two fingers missing. Living in such a close-knit community, these accidents are a constant reminder of the hazards of his occupation. Fear of developing pneumoconiosis, the incidence of which is very high in this area, may be an additional worry. In four pits in County Durham 50% of the miners over the age of 56 who had chest radiographs taken showed evidence of pneumoconiosis (McCallum, Browne, and Campbell, 1955). The miner is conscious at all times that any of these occupational hazards would entail a great reduction in his earning capacity.

It is probably his daily working conditions which provide the greatest stress of all. Continually working in semi-darkness, lacking fresh air, he is constantly inhaling coal dust. The seams are often so low that he cannot stand up, and he is always cramped, perhaps crawling on his stomach or working lying on his side for up to eight hours at a time.

Ross, Miller, Leet, and Princi (1954) have described a study of 40 miners who were hospital patients for respiratory complaints. They concluded after a thorough psychiatric examination of each case, that only 12·5% of the patients had a disability on purely physical grounds alone, and that psychoneurosis was the most significant diagnosis in one-third of their patients. They attributed this mainly to the environmental stresses of mining.

However, none of this is evidence that miners are any more neurotic than workers in other industries, and it was to determine whether this is so that this study was made.

The factor analysis has thrown some light on the reason for only three of the tests discriminating between the two groups (see Table 1). Heron 1 and leg persistence are the only tests of emotional instability to have a high loading solely on F_1. With all the other tests of emotional instability having small loadings on F_1, it seems justifiable to regard it as a factor of emotional instability.

It can be seen that hand persistence has an equally high loading on F_3, a factor orthogonal to F_1. Heron's test of unsociability also has a very high loading on F_3, and it could therefore be identified as a factor of unsociability.

The fairly high loading of the two persistence tests on F_2 suggests that this factor might be one of persistence, but it is difficult to reconcile this with the high negative loading of food aversions on this factor. The significant difference obtained between the means on the hand persistence test (the miners having greater persistence), could be interpreted as implying that they are less neurotic than the railway workers. However, it seems more likely that the significant difference obtained has a purely physical explanation in that miners are constantly using hand tools. This may also account for the scores on the leg persistence test on which the miners showed greater persistence than the railwaymen though this difference was not significant.

The results on the remaining test in the battery are not very conclusive. Fluency is the only other test to discriminate in the appropriate direction and it has not a high enough loading on F_2 to be regarded as a strong measure of emotional instability.

The factor analysis does to a certain extent support the results on the validation of the 17 psychiatric patients. Admittedly this number is small but it is remarkable that Heron's inventory was the only test to discriminate between this group and the

railwaymen. These results, together with the factor analysis, confirm Heron's (1955) view that most tests of emotional instability are also sensitive to differences on other personality dimensions. This makes it inadvisable to use them as pure measures of emotional instability.

This study has shown the difficulty of applying personality tests to different groups of people; in some instances these groups are differentiated by characteristics which themselves may selectively prejudice their responses. For example, one cannot administer a body sway test to men suffering from nystagmus since postural disturbance is itself a symptom of the disease. However, if tests which are really sound measures of a particular dimension of personality are to be used in research and clinical diagnosis, it is vital that they are insensitive to these external variables and have a basis in the more fundamental characteristics of the dimension they are supposed to be measuring.

These results justify the writer in concluding, from the results on Heron 1, that the main hypothesis concerning the stability of underground workers has been supported.

The author wishes to thank all the miners and railwaymen who took part so willingly; Dr. J. P. Child and Dr. J. J. Justice, of St. Thomas' Clinic, Newcastle upon Tyne, for providing the psychiatric group; Dr. Gray of the North-East Branch of British Railways for making it possible to test the railwaymen; Professor R. C. Browne, Dr. Alastair Heron, and Dr. N. Loveless for their criticism and advice; Mr. D. J. Newell for statistical assistance; and Mrs. D. Weightman for help with the tables and graphs.

References

Bennett, E. (1945). *Brit. J. med. Psychol.*, **20**, 271.
Eysenck, H. J. (1947). *Dimensions of Personality*. Kegan Paul, London.
Halliday, J. L. (1943). *Psychosomat. Med.*, **5**, 71.
Heron, A., and Braithwaite, D. (1953). *Brit. J. industr. Med.*, **10**, 27.
—— (1955). *Educ. Psychol. Measmt*, **15**, 117.
—— (1956). *Brit. J. Psychol.*, **47**, 243.
Lion, J. S. (1958). *Brit. J. industr. Med.*, **15**, 204.
McCallum, R. I., Browne, R. C., and Campbell, H. (1955). *Ibid.*, **12**, 279.
Ministry of Power (1956). Statistical Digest. H.M.S.O., London.
Ross, W. D., Miller, L. H., Leet, H. H., and Princi, F. (1954). *J. Amer. med. Ass.*, **156**, 484.
Wallen, R. (1945). *J. abnorm. soc. Psychol.*, **40**, 77.

Brit. J. industr. Med., 1960, **17**, 46.

THE DEVELOPMENT OF ROTARY NYSTAGMUS IN THE CAT AS A FUNCTION OF AGE

BY

N. E. LOVELESS

From the Nuffield Department of Industrial Health, University of Durham (King's College, Newcastle upon Tyne)

(RECEIVED FOR PUBLICATION FEBRUARY 3, 1959)

Although it is known that the onset of miners' nystagmus is related to the age of the worker, the nature of the relationship is difficult to determine from clinical data. An attempt has been made to clarify this relationship by the use of animal subjects. Thirty-five cats of ages ranging from 1 to 41 weeks were kept in darkness and examined regularly for oscillation of the eyeballs. The rate at which the amplitude of oscillations increased appeared to be a logarithmic function of the age at which the animal was placed in darkness. This result is discussed in relation to the mechanisms involved in the disease. A second important finding is that every animal tested developed detectable oscillations. It is suggested that the same would be true of man, given sufficient exposure to conditions of low illumination. This raises more acutely the question why incapacity resulting from the disease is found in only a minority of miners, and is not clearly related to the severity of the visual disorder.

The onset of miners' nystagmus appears to be related in some way to the age of the worker. It is commonly held to be a disease of middle age, occurring most typically after some 20 to 30 years of underground work. This statement is presumably based upon the first report of the Miners' Nystagmus Committee (1922), which includes a graph showing the ages of 2,000 certified cases at the time of onset of the disease. While this distribution ranges over the entire span of working life, it approximates closely to a normal distribution with a median age of about 40 years and a quartile deviation of about eight years. Thus, from the clinician's point of view, it is true to say that certifiable cases will most typically be men in early middle life.

This statement can, however, be misleading in that it takes no account of the fact, shown in the same graph, that the number of men employed underground decreases progressively with age. If the data given are assumed to be representative, and are re-plotted to show incidence relative to the proportion of men employed underground in each age group, the resulting curve (Fig. 1) shows no distinct peak in the middle years, but is rather a monotonic and positively accelerated function of age. It might be regarded as the early section of a normal distribution, but in this case the peak presumably falls beyond the span of working life. Thus, from the point of view of the worker rather than the clinician, the risk that he will be affected by the disease appears

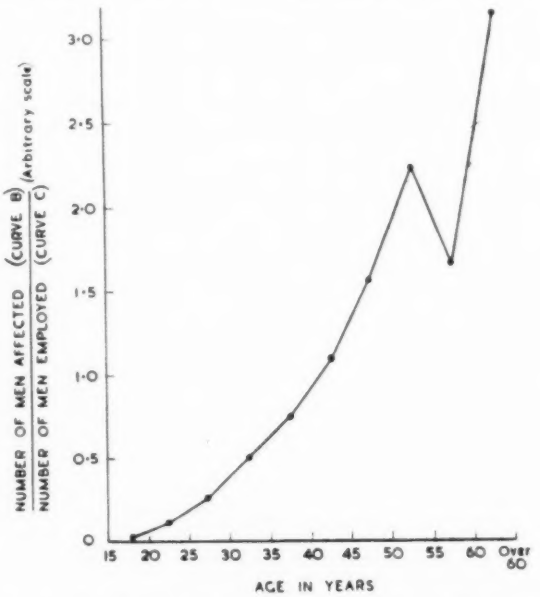


FIG. 1.—Data from Graph V of first report of Miners' Nystagmus Research Committee (1922) re-plotted to show incidence relative to numbers in each age group employed underground.

to increase continuously as long as he remains exposed to the conditions of work which produce it. It should also be noted that we cannot confidently set any limit to the proportion of men who might theoretically be affected if the working span were sufficiently prolonged.

A number of factors make it difficult to determine the relationship between age and the development of nystagmus from clinical data. There are obvious statistical deficiencies in the available data: the progressive retirement with age from work at the coalface may well be selective; the conditions of illumination in which a man has worked are not exactly known, and since the majority of miners begin work in adolescence, the effect of age cannot be separated from that of time spent underground.

The present study is an attempt to control these factors by the use of animal subjects, and so to determine the effect of age on the development of nystagmic oscillations.

Procedure

The subjects of the experiment were 37 cats. At predetermined ages between 1 and 41 weeks, they were placed in individual cages in an experimental room, where they were kept in total darkness except for a brief daily period during which they were cleaned and fed. An adequate diet and a reasonable standard of heating and ventilation were provided, but despite these precautions, two cats died of a virus infection during the course of the experiment. Complete records are therefore available only for the remaining 35 animals, which were kept in good health, apart from some muscular atrophy due presumably to lack of exercise.

The animals were inspected weekly to determine whether oscillations could be detected, first with the naked eye, then with an ophthalmoscope, and these two observations were separately recorded. The difference between the two criteria is essentially one of amplitude, since the ophthalmoscope made possible the detection of finer oscillations. It was, however, more difficult to distinguish these from the effects of head tremor and voluntary eye movement, and the experimenter felt more confidence in judgments made with the naked eye. The ophthalmoscope was also difficult to use with very young kittens because of the opacity of the optic media, the small aperture of the pupil, and the subjects' constantly changing direction of gaze.

Observations were discontinued on animals which did not produce oscillations visible with the naked eye after two to three years in darkness. The remaining animals were kept in daylight after various periods spent in darkness, and observations were made on the course of their recovery.

Analysis of Data

An estimate was made of the period spent in darkness before each of the two criteria was reached. The younger cats normally progressed fairly steadily from a state in which no oscillations could be detected to one in which oscillations could be detected only with the ophthalmoscope, and finally to one in which they were visible to the naked eye. The date at which a transition took place can therefore be stated to the nearest week. As in man, however, the amplitude of oscillation shows some fluctuation with such factors as the animal's posture and direction of gaze, and probably with its emotional state. A small number of records, mostly of older cats, do not therefore show a steady progression from week to week. In these cases a time is stated after which the given criterion is recorded with a fair degree of consistency.

The element of uncertainty involved may be illustrated by the record of cat No. 42 (Table 1). This animal was placed in darkness at the age of 20 weeks. The record for the next 30 weeks reads as follows, where S denotes steadiness of the eye, O an oscillation detectable only with the ophthalmoscope, and N an oscillation detectable with the naked eye:—S S S S S S S S O O S O O O O O O N O O O O O N N N N N N N N. The onset of oscillations detectable with the ophthalmoscope was taken as from the ninth week, despite a later negative record, and the onset of oscillations detectable with the naked eye was taken as from the twenty-fourth week, despite an earlier positive record.

Where the records show more than a transitory irregularity, this has been indicated in the results.

Results

The estimates obtained by the above procedure are presented in Table 1. It will be seen that oscillations were detected with the ophthalmoscope in all the animals, but appeared to develop more quickly in the younger cats. The majority of animals up to 15 weeks old developed oscillations visible with the naked eye, but four cats, aged 6 to 8 weeks, failed to do so, and for three of these the ophthalmoscopic records are irregular. Of four animals between 20 and 25 weeks old, three showed only a transitory episode of oscillations visible with the naked eye. No animals over 25 weeks old reached this criterion after two to three years in darkness. In the majority of the older cats, the ophthalmoscopic records show some irregularity; in a number of cases, the oscillations become sporadic after a time, and occasionally seem to have disappeared altogether.

In Fig. 2, the time taken to develop oscillations visible with the ophthalmoscope is plotted as a function of the age at which the animal was placed in darkness, the ordinate being shown on a logarithmic scale. Although the data show a considerable scatter, they yield a rank-order correlation

TABLE 1

TIME TO DEVELOP NYSTAGMUS AS A FUNCTION OF AGE OF CATS PUT IN DARKNESS

Cat No.	Litter	Sex	Age Put in Darkness (weeks)	Time to Develop Oscillations Visible with:	
				Ophthalmoscope (weeks)	Naked Eye (weeks)
15	A	M	1	7	8
16	A	F	1	6	7
17	A	F	1	5	8
12	—	M	3	6	9
10	—	M	6	49 (sporadic)	Not developed in 142
29	E	M	6	4	7
30	E	M	6	6	17
31	F	M	7	2	Not developed in 155
32	F	F	7	2	16
33	—	F	7	3	16
39	H	M	7	7 (sporadic)	Not developed in 125
40	H	M	7	4	11
13	N	M	8	5	8
14	N	M	8	30 (sporadic)	Not developed in 129
4	—	M	10	20	20
6	—	M	10	11	11
8	M	M	11	6	8
11	M	F	11	12	12
9	—	F	15	23	30 (sporadic until 54)
47	K	F	15	9	39 (sporadic)
48	K	F	15	7	29
49	K	F	15	4	25 (sporadic)
42	I	F	20	9	24
44	—	F	20	24 (sporadic)	43 (lasted only 7 weeks)
45	I	F	20	31	45 (lasted only 4 weeks)
1	—	M	23	35 (sporadic)	66 (lasted only 6 weeks)
21	C	M	28	8	Not developed in 100
22	C	M	28	20 (sporadic after 100)	Not developed in 156
23	C	M	28	15 (sporadic after 34 disappeared after 88)	Not developed in 156
18	B	M	40	15	Not developed in 148
19	B	F	40	57 (sporadic after 73 disappeared after 109)	Not developed in 156
20	B	F	40	21 (sporadic after 100)	Not developed in 156
7	—	F	41	25 (sporadic)	Not developed in 162
24	D	F	41	3	Not developed in 156
25	D	M	41	4 (sporadic after 90 disappeared after 126)	Not developed in 156

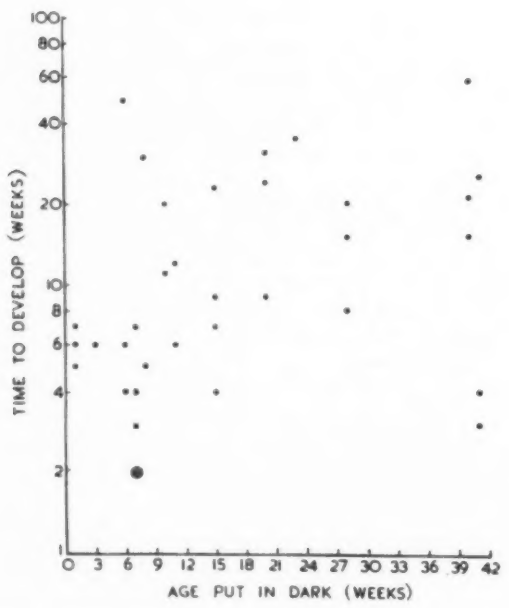


FIG. 2.—Time to develop oscillations detectable with the ophthalmoscope, as a function of age of cats put in darkness.

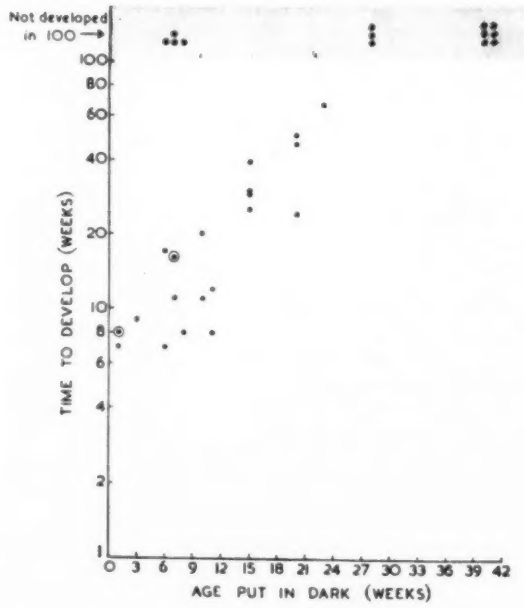


FIG. 3.—Time to develop oscillations detectable with the naked eye, as a function of age of cats put in darkness.

coefficient of + 0·39, which is significant at the 2% level of confidence.

Fig. 3 shows the same relationship for the naked-eye criterion; the cats which developed no oscillations are shown at the top of the graph. If these cases are treated as an upper terminal category, the rank-order correlation coefficient is + 0·69, which is significant beyond the 0·001% level of confidence. The trend shown on the graph is reasonably linear, suggesting that the time taken to develop oscillations of a given amplitude increases logarithmically with age.

Details of recovery rates are not presented, since the number of cases is too small to establish any definite relationship when time spent in darkness must be considered as an additional variable. It may, however, be noted that while the great majority of cats recover completely within a year, the three animals which spent 25 weeks in darkness from the age of 1 week still show gross oscillations after more than five years in daylight.

Discussion

Nystagmic oscillations appear in general to increase in amplitude at a rate dependent upon the age of the animal when placed in darkness. The four cats aged 6 to 8 weeks, which did not develop oscillations large enough to be detected with the naked eye, seem sufficiently divergent from this general trend to constitute a separate group. We can at present offer no explanation of this anomaly. It is perhaps worth noting that all four animals were male, but scrutiny of the remaining cases does not suggest that sex has any general influence on the development of the condition. Each of the four animals came from a different litter.

The fact that the relationship appears to be non-linear is of some interest. It suggests, for example, that a change in school leaving age might have a disproportionate effect upon the incidence of nystagmus, and that a measure of prevention might be attained by allocating the younger miners to the best available conditions of illumination. The plausibility of these suggestions rests, however, upon the extent to which visual development in the cat parallels that in man, and upon consideration of the mechanisms involved in the disorder.

Comparative studies of nystagmus have thrown some light on these mechanisms. Ohm (1916) produced nystagmus in dogs and cats kept in darkness, Riesen (1947, 1950) produced it in chimpanzees, and Browne (1951) was able to produce it in cats, but not in rats or rabbits. It is apparently not present in pit ponies. Susceptibility to nystagmus therefore appears to be related to the extent of the binocular field and of decussation at the optic chiasma, the ability to perform voluntary conjugate eye movements, and the possession of a diurnal eye with a well-marked area centralis. The latter feature may well be the critical factor, since the horse has a diurnal eye whose area of highest acuity forms a horizontal band rather than a central zone (Walls, 1942). In this connexion it is of interest to consider phylogenetic differences in optokinetic reactions. Eye movements in pursuit of moving striations can be elicited in vertebrates as low as the lizard, and appear to be subvortically determined. The pursuit of single objects against a dark background, however, appears to involve a different mechanism. Optokinetic reactions of this kind can be produced in dogs, cats, and monkeys, but not in rodents, and are abolished by destruction of the striate cortex. Since this operation also increases the extent of the striations of a patterned field required to elicit visual pursuit, it is plausible to suppose that it eliminates the central mechanisms of the area centralis. The absence of this type of optic nystagmus in rodents is then accounted for by their complete lack of an area of acute vision (Smith and Bojar, 1938). These facts accord with the hypothesis that miners' nystagmus involves disturbance of the normal process of fixation, as a result of life in conditions of illumination in which the macula cannot function (Davson, 1949; Ferguson, 1952). The failures of binocular vision seen in miners' nystagmus appear to be the result of oscillations rather than their cause (Campbell, Harrison, and Vertigen, 1951).

On this view, it would be expected that the effect of exposure to darkness would vary with the extent to which normal macular fixation has become established by maturation and learning. In the cat, an optokinetic response to moving striations first appears about the fourteenth day, and the width of striations necessary to produce it then decreases until about the twenty-sixth day. These developments precede the formation of precise localizing responses of the forelimbs and other behaviour requiring fine visual adjustment (Smith and Bojar, 1938). There is unfortunately no evidence on the ontogeny of optokinetic responses to single moving objects, but it is probable that movements of this type resemble binocular convergence and object recognition in requiring considerable practice for their perfection (Riesen, 1950). Those animals which have received most practice might then take longer to lose the habit when placed in darkness, and might more readily revert to it when returned to daylight. It is also likely, however, that maturational factors are of importance in the perfection of these responses. There is evidence that exposure to radiation in the first few weeks of life is necessary for the

normal development of the retina and its associated structures. It has also been shown that chicks reared in darkness and artificially fed never develop the normal pecking response (Beach and Jaynes, 1954). Thus prevention of practice at the appropriate stage of growth may interfere with the development of behaviour which appears to be instinctive or reflex in nature. It seems possible that the three cats placed in darkness at the age of 1 week similarly failed to develop normal macular fixation.

A comparable process of development takes place in man. The human infant shows some evidence of monocular fixation from birth, but sustained voluntary fixation appears to require the development of an inhibitory mechanism which does not become efficient until about the age of 4 weeks. Binocular convergence is not clearly present until about the eighth week, and it is likely that the development of oculomotor skill continues for a much longer period (Gesell, Ilg, and Bullis, 1949). It may be doubted whether any appreciable change in performance is still occurring at adolescence, but the long reinforcement which the habit has then received makes it understandable that miners develop oscillations of appreciable magnitude only after considerable exposure to conditions of low illumination.

The present experiment appears to be the first comparative study which has used an appreciable number of subjects. It seems important, therefore, to stress that every animal produced detectable oscillations, at least for a period. This strongly supports the hypothesis that defective illumination is the primary cause of the visual disorder, and makes it reasonable to suppose that every miner working in sufficiently low illumination would develop oscillations sooner or later. This conclusion seems to be in accordance with the clinical evidence, when due allowance is made for variation in lighting standards. The Miners' Nystagmus Committee reported in 1923 that the prevalence of oscillations in miners working in safety-lamp pits might then be as high as 34% of the men employed. Caiger (1941) was of the opinion that an expert observer could detect oscillations in most miners over 50 years of age.

The probability that susceptibility to oscillations is universal raises more acutely the already much-discussed problem of the extent to which the visual disorder is responsible for incapacity to work. Since normal "physiological" nystagmus does not produce instability of the visual field, and is in fact essential for seeing, it might be supposed that oscillations must build up to some critical amplitude before they become disturbing; individual differences in the rate of development might then explain why most men do not reach this stage within their working lives. Against this is the fact that men with marked oscillations may be free of symptoms. Presumably such individuals are able to adapt their visual mechanisms so as to tolerate the disorder; that such adaptation is possible is clear from the stability of the visual field in congenital nystagmus. Again, men who are aware of their oscillations often develop some skill in controlling them (Campbell *et al.*, 1951). Disablement might then be regarded as due to psychological incapacity to adapt, in one way or another, to the visual disorder. This hypothesis faces the difficulty that many certified nystagmics do not exhibit gross oscillations, but it seems possible that a considerable proportion of these suffer from defects of binocular vision which are not associated with oscillations, though they give rise to similar symptoms (Campbell *et al.*, 1951). Adaptability is likely to be itself a function of age (Welford, 1958), as well as of personality.

Most investigators agree that there is a psychological element in the disease as certified, and psychiatric experts have usually held that this factor is predominant (Culpin, 1925; Halliday, 1943; Stern, 1948). More recently, objective psychological tests have shown that men with nystagmus are less emotionally stable than men without the disease (Lion, 1958a). This is not to deny that other physical factors may affect the development of the disease. There is evidence that the symptoms are rendered more likely by work in a stooping posture (Browne and Beck, 1954). Defective dark adaptation is also associated with the disorder, though its role is unclear (Ferguson, 1952). It should, however, be noted that this condition is itself associated with emotional instability (Eysenck, 1947).

The precise role of the psychological element has been the subject of some controversy. Thus, it has been suggested (Miners' Nystagmus Committee, 1923) that the terms of certification allow the inclusion of a number of neurotic individuals without gross visual symptoms; but the psychological tests show no difference in emotional stability between certified nystagmics with and without oscillations (Lion, 1958b).

A further possibility is that the psychiatric features of the disorder are a not unjustified reaction to the disturbing visual symptoms and the threat of unemployment and financial hardship. Browne, Beck, Saint, and McCallum (1950) describe the nystagmic patient as a conscientious, quiet, family man. An individual who takes his responsibilities seriously might be regarded as more likely to react with anxiety and depression to the onset of visual symptoms.

It is not certain that the relationship of visual and emotional symptoms operates only in one direction.

It has been suggested that patients are more likely to exhibit oscillations when in a state of excitement (Shufflebotham, 1914). We believe this to be true of our experimental animals also, as exaggerated oscillations may sometimes be seen in animals startled by an extraneous noise in the course of examination. It would be of value to confirm these observations by experiment, for example, by studying the effects of an injection of adrenalin.

If emotional disturbance does increase the amplitude of oscillations, these two factors might well interact cumulatively until a breakdown is precipitated, once the visual disorder has progressed sufficiently to come to the patient's notice.

This stage may also be reached earlier in those subjects most predisposed to anxiety. Miners in general appear to show more evidence of emotional stress than the general population (Heron and Braithwaite, 1953; Lion, 1959), which is hardly surprising in view of the hazards of the occupation. Poor lighting may add to this stress, and work in conditions of reduced sensory input may in itself induce psychological disturbance (Bexton, Heron, and Scott, 1954). Those most affected by this stress may therefore develop a given amplitude of oscillation more rapidly, and the rate of development may well affect the possibility of adaptation to the disorder.

The difficulty of determining the influence of predisposition in a human population is evident, particularly when the disorder develops as slowly as in nystagmus. The possibility of investigating this aspect of the problem with animal subjects is therefore worth considering, as some progress has been made in developing measures of emotionality in animals (Broadhurst, 1957, 1958).

The author has had the advantage of discussing this paper with Professor R. C. Browne, Dr. R. I. McCallum, Mr. D. J. Newell, and Mr. D. H. Holding. The successful completion of the work owes much to the standard of animal husbandry maintained by Mr. G. E. South and his assistants.

References

Beach, F. A., and Jaynes, J. (1954). *Psychol. Bull.*, **51**, 239.
Bexton, W. H., Heron, W., and Scott, T. H. (1954). *Canad. J. Psychol.*, **8**, 70.
Broadhurst, P. L. (1957). *Brit. J. Psychol.*, **48**, 1.
——(1958). *Ibid.*, **49**, 12.
Browne, R. C. (1951). *Lancet*, **1**, 721.
——, and Beck, I. F. (1954). *Brit. med. J.*, **1**, 1176.
——, ——, Saint, E. G., and McCallum, R. I. (1950). *Brit. J. Ophthal.*, **34**, 601.
Caiger, H. (1941). *Med. Press*, **206**, 152.
Campbell, Harrison, R., and Vertigen, J. (1951). *Brit. J. Ophthal.*, **35**, 484.
Culpin, M. (1925). *Ibid.*, **9**, 564.
Davson, H. (1949). *The Physiology of the Eye*. Churchill, London.
Eysenck, H. J. (1947). *Dimensions of Personality*. Kegan Paul, Trench, Trubner and Co., London.
Ferguson, W. J. W. (1952). *Trans. Ill. Engng Soc.*, **17**, 49.
Gesell, A., Ilg, F. L., and Bullis, G. E. (1949). *Vision: its Development in Infant and Child*. Hoeber, New York.
Halliday, J. L. (1943). *Psychosom. Med.*, **5**, 71.
Heron, A., and Braithwaite, D. (1953). *Brit. J. industr. Med.*, **10**, 27.
Lion, J. S. (1958a). *Ibid.*, **15**, 204.
—— (1958b). *Brit. med. J.*, **2**, 975.
—— (1959). To be published.
Miners' Nystagmus Committee (1922). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 65.
—— (1923). *Ibid.*, No. 80.
Ohm, J. (1916). *Z. Augenheilk.*, **36**, 198.
Riesen, A. H. (1947). *Science*, **106**, 107.
—— (1950). *Scientific American*, **183**, July, p. 16.
Shufflebotham, F. (1914). *Brit. med. J.*, **1**, 648.
Smith, K. U., and Bojar, S. (1938). *Psychol. Bull.*, **35**, 193.
Stern, E. S. (1948). *Brit. J. Ophthal.*, **32**, 209.
Walls, G. L. (1942). *The Vertebrate Eye*. Cranbrook Inst. Sci. (Institute of Science), Bloomfield Hills, Michigan.
Welford, A. T. (1958). *Ageing and Human Skill*. Oxford University Press, London.

Brit. J. industr. Med., 1960, **17**, 52.

A STUDY OF HEAT STRESS IN EXTREMELY HOT ENVIRONMENTS, AND THE INFRA-RED REFLECTANCE OF SOME POTENTIAL SHIELDING MATERIALS

BY

CHARLES E. LEWIS, RICHARD F. SCHERBERGER, and FRANKLIN A. MILLER

From the Laboratory of Industrial Medicine, Eastman Kodak Company, Rochester, New York

(RECEIVED FOR PUBLICATION JUNE 22, 1959)

In the course of evaluating industrial heat exposures, three very hot environments having heat stress indices over 300 have been analysed by the techniques of Haines and Hatch (1952) and Belding and Hatch (1955). In addition, pulse and oral temperature measurements were made on three subjects exposed to these environments. These studies indicate that the methods of Haines and Hatch and Belding and Hatch tend to err on the side of safety when applied to very hot areas. Safe exposure times calculated by their techniques are approximately one-third those determined by either physiological measurement or by safe tolerance curves recommended by the American Society of Heating and Ventilation Engineers (ASHVE).

The intelligent use of shielding as a method of protecting workers from radiant heat requires a knowledge of the infra-red reflectance curves of common industrial materials. Nineteen such curves are included.

Numerous attempts have been made to translate the physical parameters of a hot environment into a physiological index which may be utilized to project the effects of that environment upon man.

One of the most successful of these attempts has been that of Belding and Hatch (1955) based upon previous work by Haines and Hatch (1952). The heat stress index which has been developed by these authors utilizes the wet-bulb, dry-bulb, and globe temperatures, the air velocity of the environment, and the metabolic heat load produced by the activity of the man.

Modern industry has created many environments which can only be classified as very hot. The heat stress index of these environments, as determined by the method of Belding and Hatch, will often be over 100 and may occasionally exceed 1,000. By definition, a Belding-Hatch heat stress index of 100 describes the maximum heat stress to which a young, healthy, acclimatized male can be subjected for eight hours without developing adverse physiological changes.

The applicability of this index to such very hot environments is not known. This report describes the analysis and study of three hot environments with heat stress indices ranging from 395 to 524 and details an attempt to analyse them by the Belding and Hatch technique.

Radiant heat frequently represents a significant percentage of the total heat load imposed by a hot environment. This poses the practical problem of shielding workers from infra-red energy. Of particular interest is the reflectance of various materials and clothing used or worn in the plant. The physician or hygienist investigating a hot process is often asked about the protective value of certain clothing or shielding. To help answer these questions, the infra-red reflecting properties of many different materials have been measured with a recording spectrophotometer. A brief report of the data so obtained constitutes the second section of this paper.

Methods

The physical characteristics of the environment were measured with a 24-hour recording device constructed in this laboratory and modelled upon a prototype developed by Dunn and McMahon at Corning Glass Works, Corning, New York (Fig. 1). The globe, dry-bulb, and wet-bulb temperatures are measured with the use of thermocouples and recorded graphically on 24-hour charts ("auto-lite" model 1000-A recording thermometers*). A small blower (Fasco No. 50747-3N)† stationed in the base of the enclosure assures a constant

* Electric Auto-lite Co., Industrial Thermometer Div., Toledo 1, Ohio.

† Fasco Ind. Inc., 255 N. Union St., Rochester 2, New York.

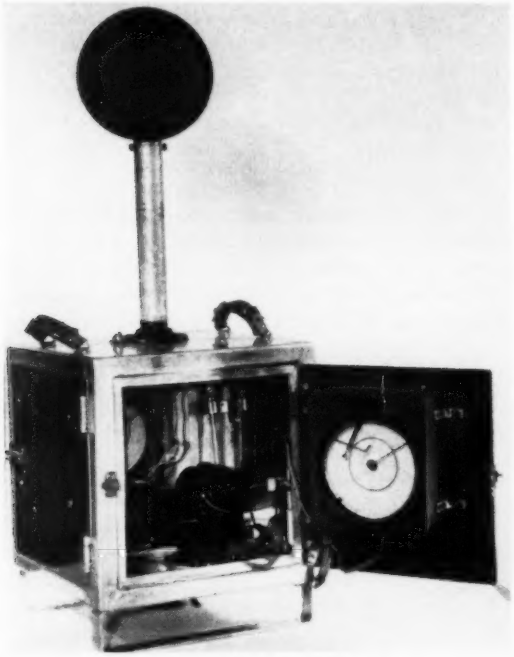


FIG. 1.—The 24-hour recording device.

air flow past the dry-bulb and wet-bulb elements. The box is constructed of aluminium to minimize the effect of radiant heat upon the dry bulb. All thermometers were checked for proper adjustment by comparison with an aspiration type psychrometer which utilized Taylor Instrument's "binoc" certified thermometers for wet- and dry-bulb temperatures. The black globe was fabricated from an 8-in. diameter, all copper, spherical, seamless float having an external lug 1 in. high which is $\frac{1}{2}$ in. coupling (standard pipe thread). This float was painted with dull black lacquer and dusted with carbon black while wet and was mounted with the centre 16 in. above the top surface of the box. In the calculation of mean radiant temperature (T_w) from globe temperature (T_g), a correction coefficient of 0·164 was used to compensate for the 8-in. diameter globe.

Air velocity was measured with the use of the model 60 "anemotherm" air meter (Anemostat Corporation of America).

Body temperatures were recorded orally before and after exposure to heat. Subjects neither smoked, drank, nor ate for one-half hour before the onset of temperature recording. Blood pressures were recorded in the left arm, utilizing an aneroid sphygmomanometer.

The Beckman DK-2 spectroreflectometer will be discussed more completely in Section II of this paper.

Subjects were unacclimatized, healthy males ranging in age from 30 to 40 and in weight from 79 to 82 kg.

Clothing worn by subjects consisted of shoes and socks, short-sleeved cotton undershirt, cotton undershorts, and light trousers.

Results: Section I

Using the environmental data given in Table 1 and the Belding-Hatch equations, heat stress indices of 524, 397, and 395 were calculated.

Area at Heat Stress Index 524.—Table 2 lists the physiological changes noted in three subjects after exposures of 15, 20, and 15 minutes in the area (A) found to have a heat stress index of 524.

All subjects noted an onset of sweating three to four minutes after entering the area. A feeling of

TABLE 1

SUMMARY OF ENVIRONMENTAL STUDIES IN HOT AREAS

Location	Modal Values of Temperatures from Recording Thermometers (°F.)			Air Velocity at Thermometer Location (ft./min.)	Sources of Heat Gain for Persons Working in this Environment (B.T.U./hr.)			E_{req} (B.T.U./hr.)	E_{max} (B.T.U./hr.)	Heat Stress Index	Maximum Exposure Time (min.)
	Wet Bulb	Dry Bulb (T_a)	Globe (T_g)		Metabolic	Radiation	Convection				
Area A (enclosed paper machine)	97	133	140	90	600*	1,123	722	2,445	467	524	7·6
Area B (2nd enclosed paper machine)	92	124	146	50	600	1,430	410	2,440	615	397	8·4
Area C (drying alley)	98	145	149	350	600	1,338	1,870	3,808	965	395	5·3

*600 B.T.U./hr. represents the metabolic heat of light, standing work.

$$C = 2\sqrt{V}\,(t_a - 95)$$

$$E_{max} = 10{\cdot}3\,V^{0{\cdot}4}\,(42 - VP_a)$$

$$R + C = (22 + 2\sqrt{V})\,(t_g - 95)$$

$$HSI = \frac{E_{req}}{E_{max}} \times 100$$

$$\text{Maximum permissible exposure (minutes)} = \frac{250}{E_{req} - E_{max}} \times 60$$

t_a = ambient temperature.
V = air speed in feet per minute.
t_g = black globe temperature.
VP_a = vapour pressure of the air in millimetres of mercury.

Brit. J. industr. Med., 1960, **17**, 52.

A STUDY OF HEAT STRESS IN EXTREMELY HOT ENVIRONMENTS, AND THE INFRA-RED REFLECTANCE OF SOME POTENTIAL SHIELDING MATERIALS

BY

CHARLES E. LEWIS, RICHARD F. SCHERBERGER, and FRANKLIN A. MILLER

From the Laboratory of Industrial Medicine, Eastman Kodak Company, Rochester, New York

(RECEIVED FOR PUBLICATION JUNE 22, 1959)

In the course of evaluating industrial heat exposures, three very hot environments having heat stress indices over 300 have been analysed by the techniques of Haines and Hatch (1952) and Belding and Hatch (1955). In addition, pulse and oral temperature measurements were made on three subjects exposed to these environments. These studies indicate that the methods of Haines and Hatch and Belding and Hatch tend to err on the side of safety when applied to very hot areas. Safe exposure times calculated by their techniques are approximately one-third those determined by either physiological measurement or by safe tolerance curves recommended by the American Society of Heating and Ventilation Engineers (ASHVE).

The intelligent use of shielding as a method of protecting workers from radiant heat requires a knowledge of the infra-red reflectance curves of common industrial materials. Nineteen such curves are included.

Numerous attempts have been made to translate the physical parameters of a hot environment into a physiological index which may be utilized to project the effects of that environment upon man.

One of the most successful of these attempts has been that of Belding and Hatch (1955) based upon previous work by Haines and Hatch (1952). The heat stress index which has been developed by these authors utilizes the wet-bulb, dry-bulb, and globe temperatures, the air velocity of the environment, and the metabolic heat load produced by the activity of the man.

Modern industry has created many environments which can only be classified as very hot. The heat stress index of these environments, as determined by the method of Belding and Hatch, will often be over 100 and may occasionally exceed 1,000. By definition, a Belding-Hatch heat stress index of 100 describes the maximum heat stress to which a young, healthy, acclimatized male can be subjected for eight hours without developing adverse physiological changes.

The applicability of this index to such very hot environments is not known. This report describes the analysis and study of three hot environments with heat stress indices ranging from 395 to 524 and details an attempt to analyse them by the Belding and Hatch technique.

Radiant heat frequently represents a significant percentage of the total heat load imposed by a hot environment. This poses the practical problem of shielding workers from infra-red energy. Of particular interest is the reflectance of various materials and clothing used or worn in the plant. The physician or hygienist investigating a hot process is often asked about the protective value of certain clothing or shielding. To help answer these questions, the infra-red reflecting properties of many different materials have been measured with a recording spectrophotometer. A brief report of the data so obtained constitutes the second section of this paper.

Methods

The physical characteristics of the environment were measured with a 24-hour recording device constructed in this laboratory and modelled upon a prototype developed by Dunn and McMahon at Corning Glass Works, Corning, New York (Fig. 1). The globe, dry-bulb, and wet-bulb temperatures are measured with the use of thermocouples and recorded graphically on 24-hour charts ("auto-lite" model 1000-A recording thermometers*). A small blower (Fasco No. 50747-3N)† stationed in the base of the enclosure assures a constant

* Electric Auto-lite Co., Industrial Thermometer Div., Toledo 1, Ohio.

† Fasco Ind. Inc., 255 N. Union St., Rochester 2, New York.

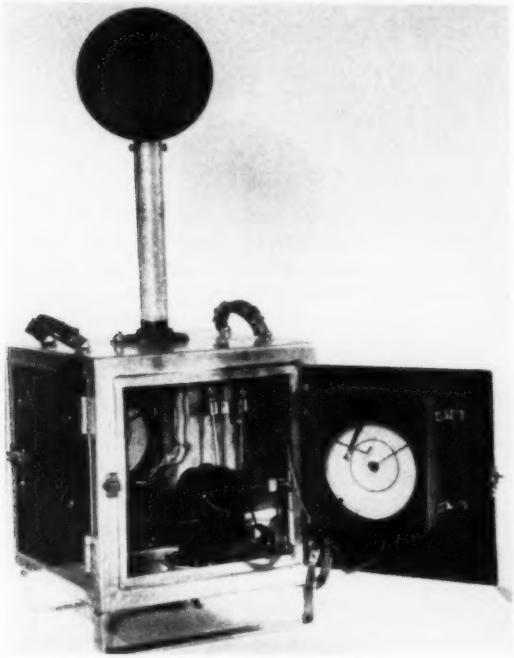


FIG. 1.—The 24-hour recording device.

air flow past the dry-bulb and wet-bulb elements. The box is constructed of aluminium to minimize the effect of radiant heat upon the dry bulb. All thermometers were checked for proper adjustment by comparison with an aspiration type psychrometer which utilized Taylor Instrument's "binoc" certified thermometers for wet- and dry-bulb temperatures. The black globe was fabricated from an 8-in. diameter, all copper, spherical, seamless float having an external lug 1 in. high which is ½ in. coupling (standard pipe thread). This float was painted with dull black lacquer and dusted with carbon black while wet and was mounted with the centre 16 in. above the top surface of the box. In the calculation of mean radiant temperature (T_w) from globe temperature (T_g), a correction coefficient of 0·164 was used to compensate for the 8-in. diameter globe.

Air velocity was measured with the use of the model 60 "anemotherm" air meter (Anemostat Corporation of America).

Body temperatures were recorded orally before and after exposure to heat. Subjects neither smoked, drank, nor ate for one-half hour before the onset of temperature recording. Blood pressures were recorded in the left arm, utilizing an aneroid sphygmomanometer.

The Beckman DK-2 spectroreflectometer will be discussed more completely in Section II of this paper.

Subjects were unacclimatized, healthy males ranging in age from 30 to 40 and in weight from 79 to 82 kg.

Clothing worn by subjects consisted of shoes and socks, short-sleeved cotton undershirt, cotton undershorts, and light trousers.

Results: Section I

Using the environmental data given in Table 1 and the Belding-Hatch equations, heat stress indices of 524, 397, and 395 were calculated.

Area at Heat Stress Index 524.—Table 2 lists the physiological changes noted in three subjects after exposures of 15, 20, and 15 minutes in the area (A) found to have a heat stress index of 524.

All subjects noted an onset of sweating three to four minutes after entering the area. A feeling of

TABLE 1

SUMMARY OF ENVIRONMENTAL STUDIES IN HOT AREAS

Location	Modal Values of Temperatures from Recording Thermometers (°F.)			Air Velocity at Thermometer Location (ft./min.)	Sources of Heat Gain for Persons Working in this Environment (B.T.U./hr.)			E_{req} (B.T.U./hr.)	E_{max} (B.T.U./hr.)	Heat Stress Index	Maximum Exposure Time (min.)
	Wet Bulb	Dry Bulb (T_a)	Globe (T_g)		Metabolic	Radiation	Convection				
Area A (enclosed paper machine)	97	133	140	90	600*	1,123	722	2,445	467	524	7·6
Area B (2nd enclosed paper machine)	92	124	146	50	600	1,430	410	2,440	615	397	8·4
Area C (drying alley)	98	145	149	350	600	1,338	1,870	3,808	965	395	5·3

*600 B.T.U./hr. represents the metabolic heat of light, standing work.

$$C = 2\sqrt{V}\,(t_a - 95)$$

$$E_{max} = 10{\cdot}3\,V^{0{\cdot}4}\,(42 - VP_a)$$

$$R + C = (22 + 2\sqrt{V})\,(t_g - 95)$$

$$HSI = \frac{E_{req}}{E_{max}} \times 100$$

$$\text{Maximum permissible exposure (minutes)} = \frac{250}{E_{req} - E_{max}} \times 60$$

t_a = ambient temperature.
V = air speed in feet per minute.
t_g = black globe temperature.
VP_a = vapour pressure of the air in millimetres of mercury.

TABLE 2

PHYSIOLOGICAL CHANGES OBSERVED IN AREA A (ENCLOSED PAPER MACHINE) WITH HEAT STRESS INDEX OF 524

	Subject 1	Subject 2	Subject 3
Exposure time (min.)	15	20	15
Pulse rate before	88	90	68
Pulse rate after	114	120	90
Pulse rate change	+26	+30	+22
Temperature (°F.) before	98·5	99·2	98·5
Temperature (°F.) after	99·4	100·0	99·3
Body temperature change	+0·9	+0·8	+0·8
Blood pressure before	142/90	120/90	120/70
Blood pressure after	144/94	118/84	128/74
Blood pressure change	+2/+4	—2/—6	+8/+4

moderate fatigue was noted by all for approximately two to four hours after the exposure to heat. During the time of exposure, subjects walked slowly back and forth within the area so that a metabolic heat production of about 600 B.T.U./hr. was probable.

It will be noted that the pulse rate rose from 22 to 30 beats per minute and oral temperature increased 0·8°F. in two subjects exposed for 15 to 20 minutes and 0·9°F. in the subject exposed 15 minutes. There was very little change in diastolic or systolic blood pressures.

Area at Heat Stress Index 397.—Physical measurements in area B are given in Table 1.

Table 3 presents the physiological changes occurring in three subjects exposed to this environment with a heat stress index of 397.

TABLE 3

PHYSIOLOGICAL CHANGES OBSERVED IN AREA B (SECOND ENCLOSED PAPER MACHINE) WITH HEAT STRESS INDEX OF 397

	Subject 1	Subject 2	Subject 3
Exposure time (min.)	15	30	22
Pulse rate before	88	86	72
Pulse rate after	128	148	120
Pulse rate change	+40	+62	+48
Temperature (°F.) before	98·0	97·9	98·0
Temperature (°F.) after	99·6	101·6	99·7
Body temperature change	+1·6	+3·7	+1·7
Blood pressure before	130/82	110/70	120/78
Blood pressure after	148/92	108/62	134/66
Blood pressure change	+18/+10	—2/—8	+14/+12

Subject 1, who was exposed to this environment 15 minutes, sustained an increase of 1·6°F. in temperature and of 40 beats per minute in pulse rate. Both diastolic and systolic blood pressures rose 10-20 millimetres. Subject 3 remained in the same environment for a total of 22 minutes. His temperature rose 1·7°F., with a concomitant pulse increase of 48 beats per minute. His systolic blood pressure rose 14 millimetres, while his diastolic pressure fell 12 millimetres. Subject 2 remained in the environment for 30 minutes. His oral temperature was elevated 3·7°F.; his pulse rose 62 beats per minute. His systolic blood pressure remained almost unchanged and there was an 8 mm. decrease in his diastolic blood pressure.

All subjects noted the onset of sweating in two to three minutes after the start of their exposure. Subject 2 also noted mild nausea after 15 minutes and became somewhat weak and dizzy just before the termination of his exposure.

Area at Heat Stress Index 395.—Data from the third Area (C) are given in Table 1. The physiological change recorded in the same three subjects after exposures of 15, 17, and 20 minutes in this area are given in Table 4.

TABLE 4

PHYSIOLOGICAL CHANGES OBSERVED IN AREA C (DRYING ALLEY) WITH HEAT STRESS INDEX OF 395

	Subject 1	Subject 2	Subject 3
Exposure time (min.)	15	17	20
Pulse rate before	90	82	76
Pulse rate after	124	110	104
Pulse rate change	+34	+28	+28
Temperature (°F.) before	98·2	98·6	98·4
Temperature (°F.) after	100·2	100·3	100·5
Body temperature change	+2·0	+1·7	+2·1
Blood pressure before	134/76	100/78	106/68
Blood pressure after	148/108	104/74	148/60
Blood pressure change	+14/+32	+4/—4	+42/—8

The physiological changes range from an increase in body temperature of 1·7°F. in 17 minutes (Subject 2) to a 2·1°F. rise (Subject 3) after 20 minutes' exposure. Pulse rate increases were from 28 beats to 34 beats per minute.

Discussion

The Belding and Hatch approach to the physiological analysis of hot environments has proved very successful in situations where the heat stress index has been below 100. Its application to areas where the calculated index greatly exceeds this number might be expected to have certain shortcomings in view of the derivation of the approach itself.

Most of the information and studies which were considered in the evolution of the Belding-Hatch index concerned men in environments where the dry-bulb temperature did not exceed 120°F. and the wet-bulb temperature was below 96°F. It will be apparent from the formula ($HSI = 100\ E_{req}/E_{max}$) that as the capacity for evaporative cooling approaches zero, the heat stress index will approach infinity. Its use in environments where this does, in fact, occur is obviously precluded.

The projection or calculation of permissible exposure within an area having a certain heat stress index is ultimately based upon the original definition of a safe tolerance limit. This has been defined as the time required to raise the pulse 40-45 beats per minute and the body temperature 2°F. Suggested

methods of evaluating hot environments are based upon the precept that physiological changes in excess of these must be avoided (Hatch, 1958).

For the experiments described herein, two methods of estimating safe exposure times were used. The first employed the tolerance contours resulting from joint studies by the American Society of Heating and Ventilating Engineers (ASHVE) and the U.S. Bureau of Mines during the years 1922-1926 (Hatch, 1958). These curves relate permissible exposure time within an environment to the dry-bulb temperature and relative humidity of that environment; permissible exposure time is based upon measured changes in rectal temperature and heart rate. The second method of estimating permissible exposure times was that of Belding and Hatch, which utilizes an estimate of the time required to cause a 2°F. increase in body temperature, and is based upon the calculated values for E_{req} and E_{max} of the environment.

A comparison of results obtained with these two methods of estimating permissible exposure times is pertinent. In areas A and B, the ASHVE curves gave permissible exposure times of approximately 20 minutes, with 15 minutes being the predicted time in area C. In contrast, the Belding and Hatch approach indicated a permissible exposure time of eight minutes in areas A and B and five minutes in area C. Physiological measurements made in our subjects during their actual exposure in these areas indicated that the ASHVE estimates were relatively correct. Since these latter estimates are themselves based upon physiological data, this agreement was to be expected.

The foregoing comparison indicates that the estimates obtained by the Belding-Hatch method are about one-third those which physiological measurements and the ASHVE curves indicate would actually be permissible. Because the Belding-Hatch technique appears to err on the side of safety, no hazardous situations should arise from its use. This discrepancy may be related to a critical assumption made by Belding and Hatch in constructing their equations. Much of the data used in deriving the heat stress index has been based on nude subjects. The assumption was made that the wearing of light clothing will have little influence upon the heat exchange of the body by conduction and convection. This assumption is evidently valid in environments in which the heat stress index is below 100, as is evidenced by the applicability of the index in such situations (Turner, 1957). However, when the thermal gradient between skin and environmental temperature is markedly increased, the wearing of even light clothing appears to have a significant effect upon the index value.

The quantity of heat transferred to man from the environment is dependent upon the thermal conductivity of both atmosphere and clothing and upon the thickness of the still air layers. The insulating effect of a still air layer is proportional to its thickness and inversely related to the square root of the ambient air velocity (Newburgh, 1949). When the difference between air and skin temperatures is small, the reduction in heat transfer due to the insulating properties of clothing is relatively insignificant. However, as the skin-air thermal gradient increases, the still air and clothing strata may insulate the body from a significant quantity of environmental heat.

When applying this mode of heat analysis, one must be cautious not to equate heat stress indices with permissible exposure times. Note the following theoretical example, comparing two situations with different E_{req} and E_{max} but equal heat stress indices.

	1	2
E_{req} (BTU/hr.)	1,000	4,000
E_{max} (BTU/hr.)	500	2,000
Heat stress index	200	200
Permissible exposure time (min.)	30	7·5

The heat stress indices appear to indicate that the two areas are equally hot. In fact, area 2 is four times as hot as area 1 in so far as its effect upon an exposed individual is concerned. The heat stress index is based on the ratio of E_{req} to E_{max} whereas the permissible exposure time is based on the ratio of 250 to the absolute difference between E_{req} and E_{max}.

In exposures of short duration, the change in body temperature should be the most critical measurement of heat load. The pulse and blood pressure responses can be influenced by other non-thermal factors such as discomfort and anxiety. The variation in pulse rate change is obvious within and between the three areas. Other reports (Bass and Henschel, 1956) have cited the variability in blood pressure responses seen in thermal stress.

The correspondence between the permissible time estimated from the ASHVE safe tolerance contours and those actually found in the field should not be surprising. They both use the same physiological criteria.

The information obtained by physiological measurements in hot environments can be used to outline medical controls necessary to insure the health of the workers who may of necessity be required to work briefly in such environments. These medical controls include the limiting of exposure to young, healthy males who are examined by a physician at least every six months. The

maximum time spent by any one individual in the environment should be limited to a time period less than that found to cause an elevation of body temperature of 2°F. and a pulse increase of 45 beats per minute. A rest period should be provided for workers who have sustained an exposure to heat immediately after their exposure.

When job requirements are such that the time required to do the necessary tasks exceeds that of the permissible exposure, it would be necessary to utilize more than one individual, or else provide some type of direct personal protection for the individual, such as reflective clothing or air supplied suits.

While the information obtained in such physiological measurements is on men unacclimatized to heat, this would seem to be appropriate. It is highly unlikely that individuals sustaining only heat exposure of this degree would ever become acclimatized, for this, by definition, requires the performance of work within hot environments.

Section II

One of the advantages of the Belding and Hatch analysis of hot environments is that it yields values for the individual components of heat stress—radiation, convection, and conduction heat gains—and includes an estimate of evaporative heat losses.

In areas A and B, described in Section I, approximately 50% of the total heat burden incident upon an individual is due to radiation. To cool a worker in such an area, it is appropriate to apply methods which would decrease the radiation gain by reducing infra-red radiation at its source, or by reflecting it from the individual.

The quantity and wavelength distribution of infra-red energy which is radiated from a body is directly dependent upon the temperature of that body. Wien's law indicates that a body with a surface temperature of 1,200-1,400°C. will produce infra-red radiation with a mean wavelength of approximately 1·8 microns. The distribution curve of infra-red radiation from bodies with a surface temperature of about 300°C. is very flat with a mean at approximately 5 microns (Duff, 1937).

Information on the percentage reflectance at different wavelengths of infra-red energy by certain materials has been limited to the data originally derived by Coblentz (National Bureau of Standards) in the period 1917-1920 (Coblentz, 1920). Measurements of absolute infra-red reflectance are difficult and have been abandoned by many groups of investigators.

Within the past five years, an instrument has been developed which makes it possible to measure relative reflectance of radiation from the ultraviolet range up to 2·7 microns. This instrument (Beckman DK-2 spectroreflectometer) utilizes a tungsten source for the infra-red energy. Two incident monochromatic beams are used. One is

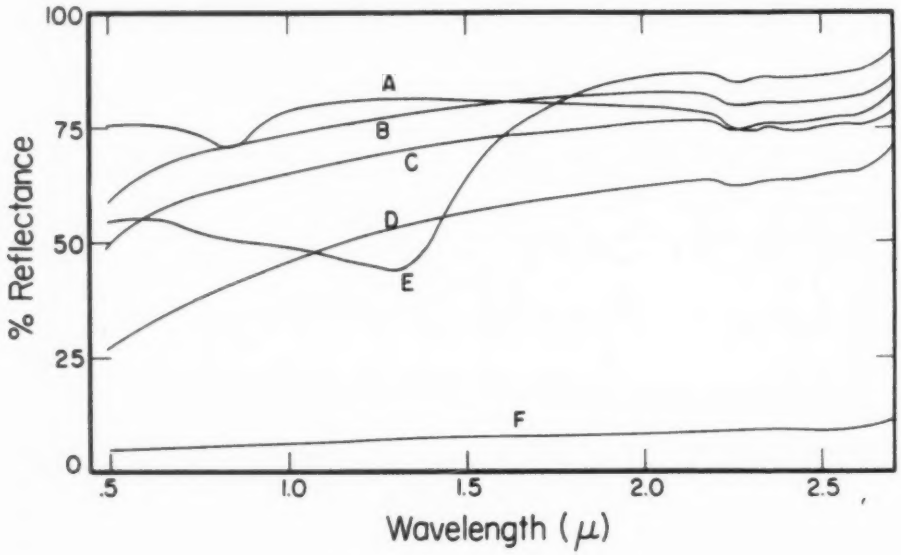


FIG. 2

A = aluminium foil.
B = buffed nickel plate.
C = nickel plate.
D = electroless nickel plate.
E = cadmium plate.
F = black paint on nickel.

directed at the reflectance standard, magnesium oxide; the other is incident on the material to be studied. The reflected energy is collected by the use of an integrating sphere and a comparison between the magnesium oxide reflectance and the unknown is recorded on the chart. The magnesium oxide reflects about 95% of infra-red energy in the range 1·0 to 2·5 microns wavelengths. To derive "absolute" reflectance values, a suitable correction must be made.

Figs. 2 to 6 demonstrate the reflectance curves of various metals, painted surfaces, and fabrics. The

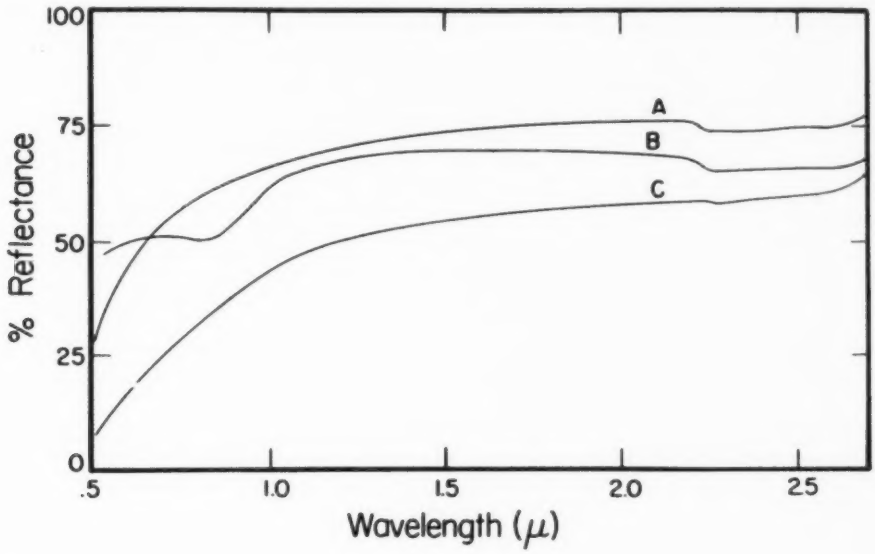


FIG. 3 A = brass. B = aluminium. C = copper.

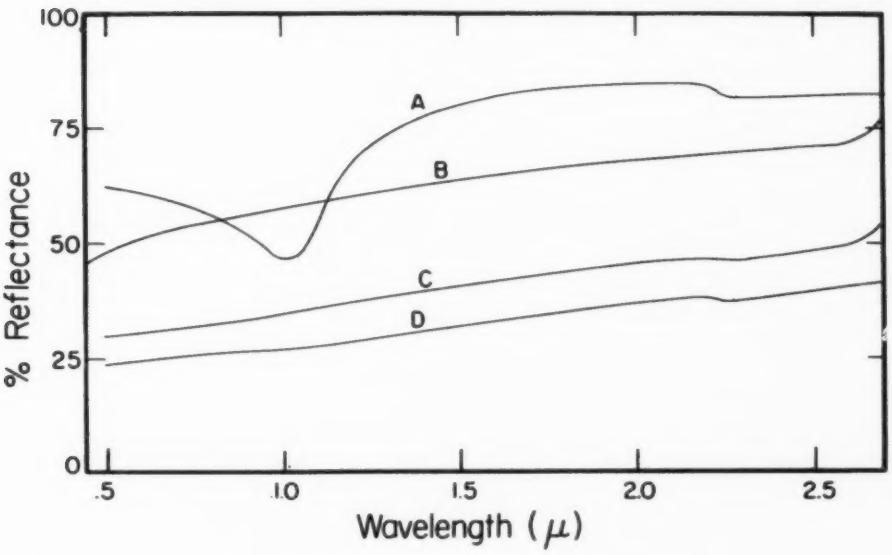


FIG. 4 A = galvanized steel. B = stainless steel. C = galvaneal. D = steel.

percentage reflectance at several specific wavelengths has been tabulated in Table 5. All materials studied, including fabrics, were backed by a black cloth to eliminate any reflection of radiation which might penetrate through the thickness of material.

It will be noted that, with respect to their percentage reflectance of wavelengths above 2·0 microns, materials tested rank in the following descending order: cadmium plate, galvanized steel, buffed nickel plate, aluminium foil. Industry, giving consideration to purchase price and ease of maintenance, has adopted aluminium as the preferred

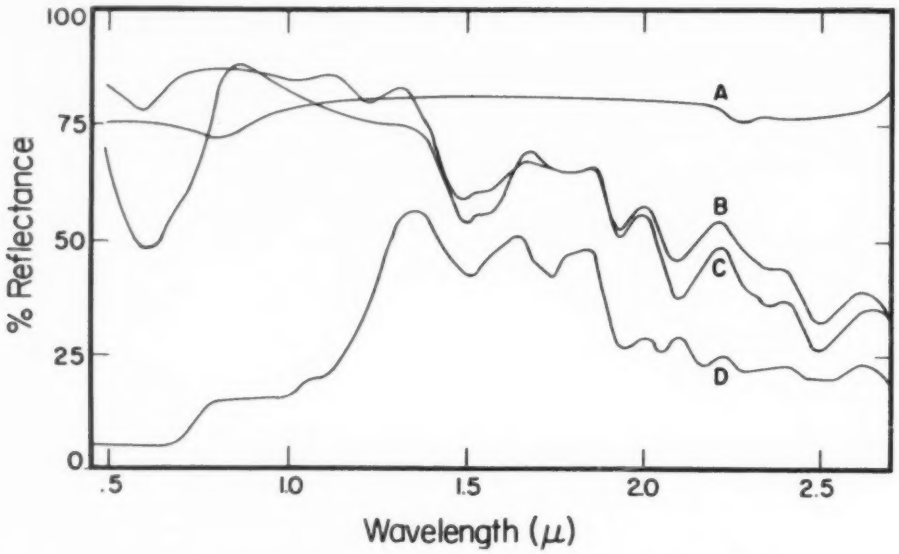


FIG. 5 A = aluminium coating reflecting fabric.
B = blue oxford cloth.
C = white broadcloth.
D = charcoal grey flannel cloth.

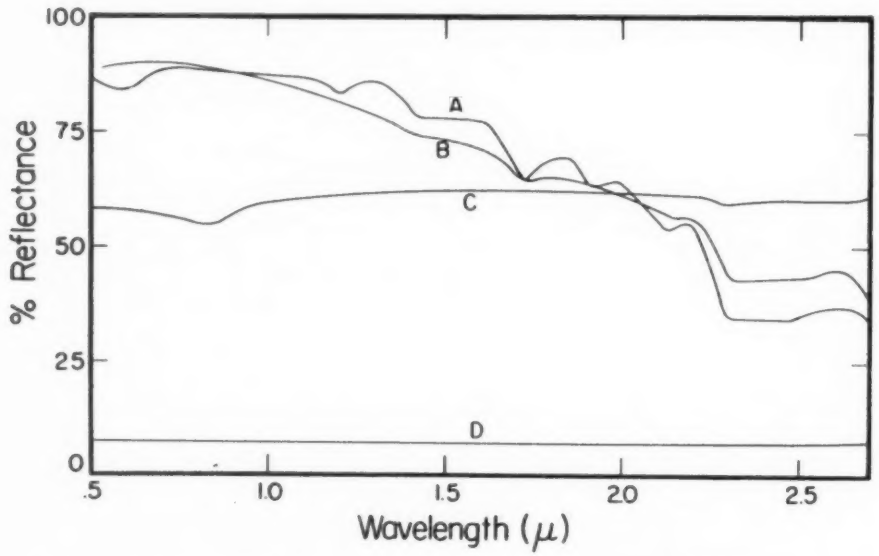


FIG. 6 A = white rubber base enamel.
B = white machine enamel on masonite panel.
C = aluminium interior varnish.
D = flat black enamel.

shielding material. While the white fabric and blue fabric are quite efficient reflectors in the near infra-red region of 1 micron, their reflectant properties decrease considerably as the wavelength exceeds 2 microns.

TABLE 5

PERCENTAGE REFLECTANCE OF VARIOUS MATERIALS AT CERTAIN WAVELENGTHS

Material	Percentage Reflectance at Certain Wavelengths				
	0·5 μ	1·0 μ	1·5 μ	2·0 μ	2·5 μ
Nickel plate-buffed	58	72	79	82	81
Electroless nickel plate	27	44	56	62	65
Nickel plate	49	64	71	76	77
Black paint on nickel	4	5	7	8	8
Cadmium plate	54	49	62	86	87
Aluminium foil	76	78	81	80	81
Aluminium	46	62	69	69	66
Brass	28	66	74	76	75
Copper	8	44	55	58	60
Steel	23	27	32	36	39
Stainless steel	45	58	63	68	71
Galvanized steel	62	46	79	85	82
Galvaneal	29	35	40	45	48
Aluminium varnish (interior)	58	59	62	62	60
White machine enamel on masonite	88	87	78	64	43
White rubber base enamel	91	85	74	61	44
Flat black enamel	7	7	7	7	7
White shirt (close cotton weave)	83	84	54	56	26
Blue shirt (oxford cloth)	70	82	59	58	32
Charcoal grey flannel	5	16	42	27	20
Reflective hood	75	78	81	81	77

Discussion

It is not possible to relate the relative reflectance in the visible range (as observed with the naked eye) to the infra-red reflectance of the same material. The above figures offer several examples of this. Values obtained with the reflectance spectrophotometer are relative to a commonly used standard (magnesium oxide) and are not absolute values. This does not negate the instrument's usefulness. Such measurements can be used to design stationary and mobile shielding as well as personnel protective equipment.

Conclusions

Three hot environments with heat stress indices of 524, 397, and 395 (as calculated by the Belding and Hatch approach) have been studied. Physiological measurements on men exposed to these environments have been made in an effort to estimate safe exposure times. Observed responses corresponded well to those predictable from the safe tolerance contours obtained by the studies of the American Society of Heating and Ventilating Engineers and the U.S. Bureau of Mines. In contrast, the calculated safe exposure times derived by the method of Belding and Hatch were found to be approximately one-third those actually measured. It is probable that this difference (between the predicted and observed permissible exposure times) is proportional to the time required for an exposed individual's peripatetic micro-environment to equilibrate with the macro-environment. The time required to reach this state of thermal equilibrium is a function of the insulating properties of his clothing. It is apparent also that with heat stress indices over 100, the simple index alone cannot provide an estimate of the safe tolerance time. Until further data are developed which make it possible to modify this index and extend it to areas such as described herein, it would seem advisable to rely upon physiological measurements as a means of evaluating the tolerance limits of very hot environments.

In Section II measurements are given on the relative reflectance of certain materials useful for shielding workers against infra-red radiation. The use of the reflectance spectrophotometer in obtaining measurements of reflectance at various wavelengths in the infra-red would seem useful in the pre-construction evaluation of equipment to be used in both mobile and stationary shielding and in personal protective equipment.

The authors are indebted to Mr. Frank Grum and Mr. Theodore Wightman, of the Eastman Kodak Company Research Laboratory, for performing the spectrophotometric measurements of infra-red reflectance.

References

Bass, D. E., and Henschel, A. (1956). *Physiol. Rev.*, **36**, 128.
Belding, H. S., and Hatch, T. F. (1955). *Heating Piping, and Air Conditioning*, August, pp. 129-136.
Coblentz, W. N. (1920). *Bulletin No.* 379, U.S. Bureau of Standards.
Duff, A. W., ed. (1937). *Physics*, 8th ed., p. 273. Blakiston, Philadelphia.
Haines, G. F., and Hatch, T. (1952). *Heating and Ventilating*, **49**, No. 11, p. 93.
Hatch, T. F. (1958). In *Industrial Hygiene and Toxicology*, ed. Patty, F. A., 2nd ed., Vol. 1, p. 806, Interscience Publishers, New York.
Newburgh, L. H. (1949). *Physiology of Heat Regulation and the Science of Clothing*. W. B. Saunders, Philadelphia.
Turner, D. (1957). *Brit. J. industr. Med.*, **14**, 177.

Brit. J. industr. Med., 1960, **17**, 60

EXCRETION OF TRICHLOROETHYLENE METABOLITES IN HUMAN URINE

BY

B. SOUČEK and D. VLACHOVÁ

From the Institute of Industrial Hygiene and Occupational Diseases, Prague

(RECEIVED FOR PUBLICATION FEBRUARY 23, 1959)

Five healthy subjects were exposed to known concentrations of trichloroethylene (T.R.I.) for five hours. The amount retained was calculated. The excretion of the metabolites monochloroacetic acid (M.C.A.), trichloroacetic acid (T.C.A.), and trichloroethanol (T.C.E.) in the urine was measured over the next seven to 14 days. Metabolites excreted represented an average of 73% of the dose of T.R.I. retained (M.C.A. 4%, T.C.A. 19%, T.C.E. 50%). The amount and speed of excretion of metabolites in one experiment was increased by giving glucose and insulin. The diurnal variation in the excretion of T.C.A. is emphasized.

After the vapour of T.R.I. has been inhaled the metabolites T.C.A., and M.C.A. are excreted in the urine. Trichloroacetic acid was first detected in canine and human urine by Barrett and Johnston (1939) and Barrett, Cunningham, and Johnston (1939), trichloroethanol was found in canine urine by Butler (1948) and in human urine by Souček and Vlachová (1954). These authors also found monochloroacetic acid to be excreted.

A number of quantitative studies of the formation of the metabolites of T.R.I. have been made. Most interest has been taken in trichloroacetic acid. The prolonged excretion (10 to 14 days) of T.C.A. even after a single exposure to T.R.I. is striking (Barrett *et al.*, 1939; Forssman, 1945; Forssman and Ahlmark, 1946; Souček and Pavelková, 1953). The excretion of the sodium salt of T.C.A. introduced into the organism is equally slow (Powell, 1945; Ahlmark and Forssman, 1949) and has not been satisfactorily explained. Fabre (1949) and Fabre and Truhaut (1952) assumed that it became linked to the red cells but experiments *in vitro* by Souček (1955) did not confirm this view although linkage to the plasma proteins was considered possible (Souček, 1954).

The gradual increase of the T.C.A. concentration in the plasma and urine for some time after the end of the exposure to T.R.I. is similarly unexplained. Ahlmark and Forssman (1949, 1951) found the excretion of T.C.A. began two to four hours after the beginning of exposure but Souček, Teisinger, and Pavelková (1952) showed that it could be detected within a few minutes. Thereafter it is agreed that the concentration of the T.C.A. in the urine rises to a maximum at 24 to 48 hours and subsequently decreases exponentially for a number of days.

The amount of T.C.A. formed from retained T.R.I. appears to vary with the species. In dogs the T.C.A. excreted accounts for 5-8% of the T.R.I. (Barrett *et al.*, 1939); in rats for 4% (Forssman and Holmquist, 1953); in rabbits for 0·5% (Bartoníček and Souček, 1959). In man higher values have been found: 6-16% (Ahlmark and Forssman, 1951); 7-27% (Souček *et al.*, 1952); 13% (Grandjean, Münchinger, Turrian, Haas, Knoepfel, and Rosenmund, 1955).

Trichloroethanol was shown by Butler (1949) to be eliminated in dogs mainly bound to glucuronic acid, and the amount excreted was three to four times that of T.C.A. The relationship of T.C.A. to T.C.E. has been found in man to be 1 : 2 to 1 : 4 (Souček and Vlachová, 1954); 1 : 2 to 1 : 7 (Teisinger, Stýblová, and Vlachová, 1955); 1 : 0·5 to 1 : 5 (Bardoděj and Krivucová, 1958).

In this paper we have investigated the quantitative relationships of the formation, and the course of elimination in the urine of all three trichloroethylene derivatives following inhalation of its vapour.

Experimental Methods

Seven experiments were carried out on three men and two women of an average age of 21 years, who previously had never come into contact with T.R.I. The test subjects inhaled the vapour of T.R.I. continuously for five hours in an exposure chamber in which the con-

centration was maintained at a constant level (± 6%) during the experiment. The concentrations of T.R.I. used in the individual tests were: 500, 850, 820, 530 μg./l. In one experiment the same individual was exposed for three successive days to concentrations of 570, 590, and 440 μg./l. During the last two hours of the exposures the concentrations of T.R.I. in the expired air of the subjects were determined, and from these data and from the concentrations of T.R.I. in the inhaled air the quantity of T.R.I. retained by the exposed individual was calculated (Souček *et al.*, 1952).

During the exposure period and the following three days all the urine was collected and analysed. In the later stages of desaturation 24-hour specimens of urine were analysed. The estimation of the metabolites was continued as long as the analytical methods permitted. In one subject the effect of administering intravenously 60 ml. of a 20% solution of glucose and 15 units of insulin at the end of the exposure was investigated. It is known that after administration of glucose with insulin the ethanol level in the blood diminishes more rapidly than under normal conditions. For this reason, it was of interest to find out whether glucose and insulin would also influence the rate of excretion of trichloroethanol, or perhaps the entire metabolism of T.R.I.

Determination of Monochloroacetic Acid.—Twenty-five millilitres of urine were acidified with 1 ml. of concentrated sulphuric acid and extracted five times with equal quantities of ethyl ether. The combined extracts were shaken with 1 ml. of pyridine, the ether evaporated under vacuum and the residue made up with water to 2·5 ml. From this concentrated extract a measured quantity was put on Whatman No. 4 chromatographic paper and developed descendingly by a 1 : 1 mixture of pyridine and amyl alcohol saturated with water. Simultaneously, a standard solution of monochloroacetic acid was subjected to the same chromatographic procedure. The position of the standard spot was detected with a solution of 0·1% methyl red in 60% ethanol adjusted to *p*H 6·5 with a drop of NaOH solution; it appears as a pink stain on a yellow background. According to the position of the standard spot the appropriate area is cut out from the chromatogram, and the organically bound chlorine determined by the method of Judah (1949), modified by Vlachová (1955). The principle of the method is as follows. Organically bound chlorine is oxidized by heating with silver dichromate in concentrated sulphuric acid. The liberated chlorine is transferred by a stream of nitrogen into a solution of potassium iodide, where it liberates an equivalent quantity of iodine, which is estimated colorimetrically after adding a solution of starch. This method permits the determination of 3μg. of chlorine with an accuracy of 97 ± 6%. It was possible to determine monochloroacetic acid in urine with an accuracy of 87 to 115%, the minimum measurable amount being 30 μg.

Determination of Trichloroacetic Acid.—To 2 ml. of urine was added 8 ml. of pure pyridine and 5 ml. of a 20% solution of sodium hydroxide. The mixture was shaken, heated for 15 minutes in a water-bath at 70°C. and then cooled in ice water; 7·5 ml. of the coloured pyridine layer was withdrawn with a pipette, clarified with 3 ml. of water and the extinction determined at a wavelength of 530 mμ in a Coleman junior spectrophotometer. The accuracy of the determination is 97 ± 5%; the minimum measurable concentration is 2μg. in 1 ml. of urine.

Determination of Trichloroethanol.—The modified method of Butler (1949) was employed. A 10 ml. sample of urine was acidified with 1 ml. of concentrated sulphuric acid and heated in a sealed tube for 14 hours in a water-bath at 90°C. The tube was opened and to 2 ml. of the sample was added 0·5 g. of an anion exchanger (OAL of the Stalin Works, Zaluzi near Most, Czechoslovakia) and the mixture shaken for 10 minutes. The trichloroacetic acid is quantitatively retained on the anion exchanger, while the trichloroethanol, liberated by the preceding hydrolysis from its linkage to glucuronic acid, remains in solution. To 0·2 ml. of the supernatant was added 0·8 ml. of an oxidizing mixture (2g. $K_2Cr_2O_7$ + 70 ml. concentrated H_2SO_4 + 30 ml. H_2O) and left for one hour at room temperature. Trichloroethanol is oxidized to trichloroacetic acid, which was estimated colorimetrically as above. The minimum measurable concentration is 10 μg. in 1 ml. of urine and the accuracy of the determination 92-102%. The hydrolysis of trichloroethanol glucuronide is accompanied by some loss, so that only 70% of the total trichloroethanol can be determined. The values of trichloroethanol were therefore multiplied by the factor 1·43.

Since this work was carried out, Vlachová (1957) has elaborated a new method for the determination of trichloroethanol in the presence of trichloroacetic acid, permitting the estimation of trichloroethanol in urine with an accuracy of 100 ± 4·5%, the limit of detectability being 1μg.

Results

The test subjects retained 630-1,280 mg. (average 915 mg.) of T.R.I., representing 58-70% (average 64%) of T.R.I. inhaled during exposure. The individual metabolites were excreted as follows:—

Monochloroacetic Acid.—This substance appears in the urine a few minutes after the beginning of the inhalation of T.R.I. vapour. The quantity in the urine increases rapidly, attaining a maximum immediately after the end of exposure, after which it falls exponentially. The total quantity excreted was 30-75 mg. (average 50 mg.) representing an average of 4% of the quantity of T.R.I. retained in the organism. The excretion continued for 48 to 168 hours (average 112 hours) after the end of the exposure. The half-period of excretion was about 15 hours. The course of excretion is shown in Fig. 1, curve 1.

Trichloroacetic Acid.—This acid appears in the urine immediately after the beginning of the inhalation of T.R.I. vapours and its concentration rises slowly; the maximum excretion was attained

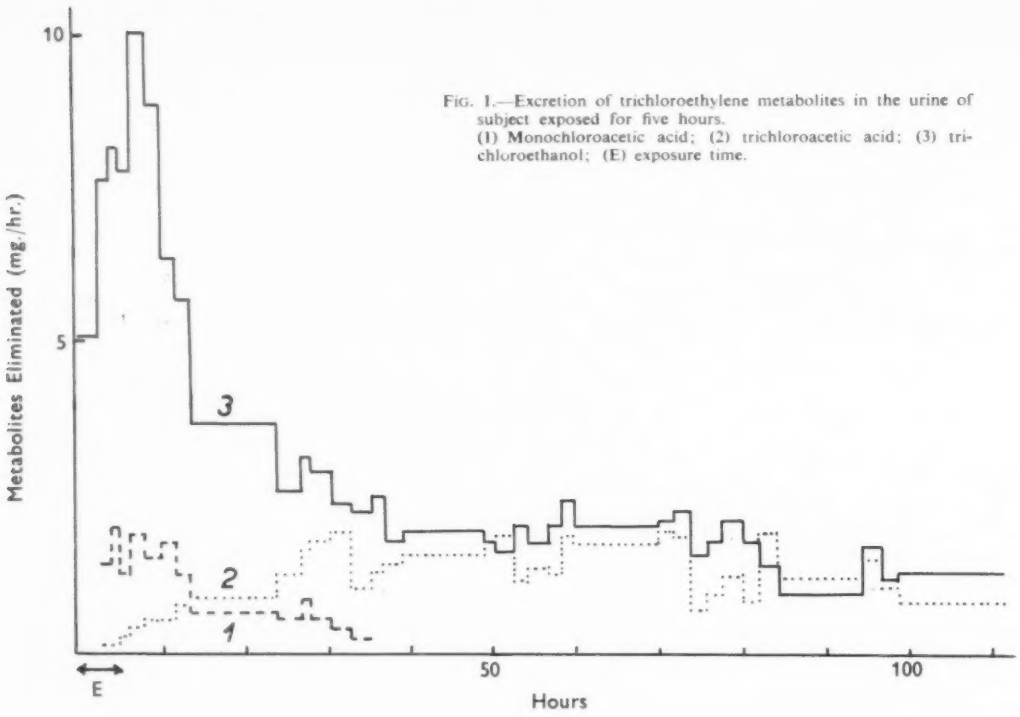


FIG. 1.—Excretion of trichloroethylene metabolites in the urine of subject exposed for five hours.
(1) Monochloroacetic acid; (2) trichloroacetic acid; (3) trichloroethanol; (E) exposure time.

within 24 hours in four experiments and within 48 hours in three others. After attaining the maximum, the fall in the rate of excretion could be analysed into the sum of two exponential rates.

The total quantity excreted was 120-560 mg. (average 260 mg.) representing 10-30% (average 19%) of the quantity of T.R.I. retained. Excretion lasted 312 to 520 hours (average 387 hours). The average half-period of excretion was 50 hours in the first phase, which lasted about five days, and 70 hours in the second phase, which lasted about 14 days.

The curve 2 in Fig. 1 shows the course of excretion of T.C.A. in one of the experiments, where the three metabolites were determined in each portion of urine excreted over a period of 110 hours from the termination of exposure. A feature of the excretion of T.C.A. is the periodicity; the amount in the urine reaches a maximum at 1300 hours each day, falls and rises again. These changes in the concentration of T.C.A. were not connected with the urine flow which varied only quite insignificantly.

Trichloroethanol.—This metabolite also appears in the urine very soon after the beginning of the inhalation of T.R.I. vapour. The quantity excreted rises rapidly, attaining its maximum a few hours after the end of exposure; its concentration then falls exponentially as the sum of two rates, a fast one at the beginning followed by a slower one.

The total quantity of T.C.E. excreted amounted to 415-655 mg. (average 520 mg.), representing 32-59% (average 50%) of the quantity of T.R.I. retained. The metabolite was excreted for 312 to 390 hours (average 350 hours). The average half-period of excretion was 24 hours in the first phase, which lasted three to four days, and 40 hours in the second phase, which lasted seven to nine days.

The concentration of T.C.E. in the individual urine specimens did not exhibit such a remarkable fluctuation in the course of the day as the concentration of T.C.A. (Fig. 1, curve 3).

The total quantity of all three metabolites excreted in the urine amounted to 43-101% (average 73%) of T.R.I. retained in the organism. The individual metabolites representing M.C.A. 4%, T.C.A. 19% and T.C.E. 50% give a ratio of approximately M.C.A. : T.C.A. : T.C.E. = 1 : 5 : 12.

In one experiment, glucose administered with insulin exerted a distinct influence on the total quantities of the three metabolites excreted. One man was exposed for five hours to T.R.I. concentrations of 500 and 530μg./l., respectively; the quantities of T.R.I. retained amounted to 770 and 860 mg. respectively and the percentage of each metabolite excreted was as follows:

Experiment		M.C.A. (%)	T.C.A. (%)	T.C.E. (%)
1	T.R.I. alone	5	30	45
2	T.R.I. followed by glucose and insulin	6	37	55

The giving of glucose and insulin caused an overall increase of approximately 22% for all metabolites excreted. On the first day after exposure the quantity of T.C.E. excreted was 2·6 times that excreted on the first day after exposure to T.R.I. alone. The quantity of T.C.A. was not noticeably influenced on the first day of excretion nor was the total duration of excretion of the metabolites influenced by the administration of glucose with insulin.

Discussion

The quantity of T.C.A. excreted after exposure of our subjects to T.R.I. vapours is in agreement with the findings in our earlier work and with those of other authors mentioned in the introduction. Considerable individual fluctuations in the quantities of this metabolite excreted were again confirmed. The causes of the periodic fluctuations of the T.C.A. concentration in the individual specimen of urine passed in the course of the day cannot be explained but show the inappropriateness of judging the level of exposure to T.R.I. from the quantity of T.C.A. found in an arbitrary sample of urine. For this purpose it is always necessary to analyse the total urine excreted during 24 hours in order to obtain significant results.

These experiments have again confirmed that the total quantity of T.C.E. excreted by man is approximately double that of T.C.A. This ratio applies to the total quantity of both metabolites excreted after a given exposure to vapours of T.R.I. This ratio, however, cannot be judged from the quantities found in single arbitrary samples of urine.

Monochloroacetic acid is only formed in quantities much lower than those of T.C.A. and T.C.E. Since M.C.A., however, is unquestionably the most toxic of the metabolites hitherto investigated, a certain significance could be ascribed to it in the overall toxicity of T.R.I.

According to Marhold (1953), the L.D.50 of some metabolites of T.R.I. for white mice when compared with that of sodium acetate are as follows:

	L.D.50 (g./kg.)
Sodium monochloroacetate	0·109 ± 0·050
Trichloroethanol	0·201 ± 0·012
Sodium acetate	0·404 ± 0·015
Sodium trichloroacetate	2·37 ± 0·11

The excretion of monochloroacetic acid from the organism proceeds fastest, that of trichloroethanol more slowly, and that of trichloroacetic acid is slower still. The half-periods of excretion (in hours) are approximately as follows:

	M.C.A.	T.C.E.	T.C.A.
First phase	15	24	50
Second phase	—	40	70

These rates of excretion seem to be comparatively constant. The slow excretion of T.C.A. is generally known for both man and various animals. The average excretion time of T.C.E. has been found to be 24 hours (20 to 29 hours). The data of Přerovská, Srbová, and Stýblová (1958), who investigated the excretion of T.C.E. after administration of T.R.I. by mouth, suggests a half-period of 28 hours; Bartoníček and Souček (1959), experimenting on rabbits, found an average half-period of 20 hours (14 to 26 hours).

Excretion and formation of T.R.I. metabolites can be influenced by drugs. According to Forssman, Owe-Larsson, and Skog (1955), the excretion of T.C.A., after giving T.R.I. to dogs and rats, drops practically to zero after administration of tetraethylthiuram disulphide (T.E.T.D.—"antabuse"). It is known that T.E.T.D. inhibits the oxidation to acetic acid of acetaldehyde in the organism. The finding of Forssman *et al.* could therefore be explained by assuming an inhibition of oxidation processes by which T.C.A. is formed from one of its possible precursors such as trichloroethanol or chloral, which in turn are formed in the organism from T.R.I. Administration of glucose with insulin, on the other hand, increases the quantity of excreted metabolites and thus influences the metabolism of T.R.I. in a positive sense. These findings could perhaps be utilized to influence the toxicity of T.R.I. or to influence the course of poisoning by this substance. Further research must decide whether inhibition or acceleration of the oxidation of T.R.I. or of its metabolites would be better suited for this purpose.

References

Ahlmark, A., and Forssman, S. (1949). Proc. IX. Int. Congr. Industr. Med., London, 1948, p. 552.

——, —— (1951). *Acta physiol. scand.*, **22**, 326.

Bardoděj, Z., and Krivucová, M. (1958). *Čsl. Hyg.*, **3**, 268.

Barrett, H. M., and Johnston, J. H. (1939). *J. biol. Chem.*, **127**, 765.

——, Cunningham, J. C., and Johnston, J. H. (1939). *J. industr. Hyg.*, **21**, 479.

Bartoníček, V., and Souček, B. (1959). *Arch. Gewerbepath. Gewerbehyg.*, **17**, 283.

Butler, T. C. (1949). *J. Pharm. exp. Ther.*, **95**, 84.

Fabre, R. (1949). Proc. IX. Int. Congr. Industr. Med., London, 1948, p. 546.

——, and Truhaut, R. (1952). *Brit. J. industr. Med.*, **9**, 39.

Forssman, S. (1945). *Svenska Läk.-Tidn.*, **42**, 1964.

——, and Ahlmark, A. (1946). *Nord. Med.*, **30**, 1033.

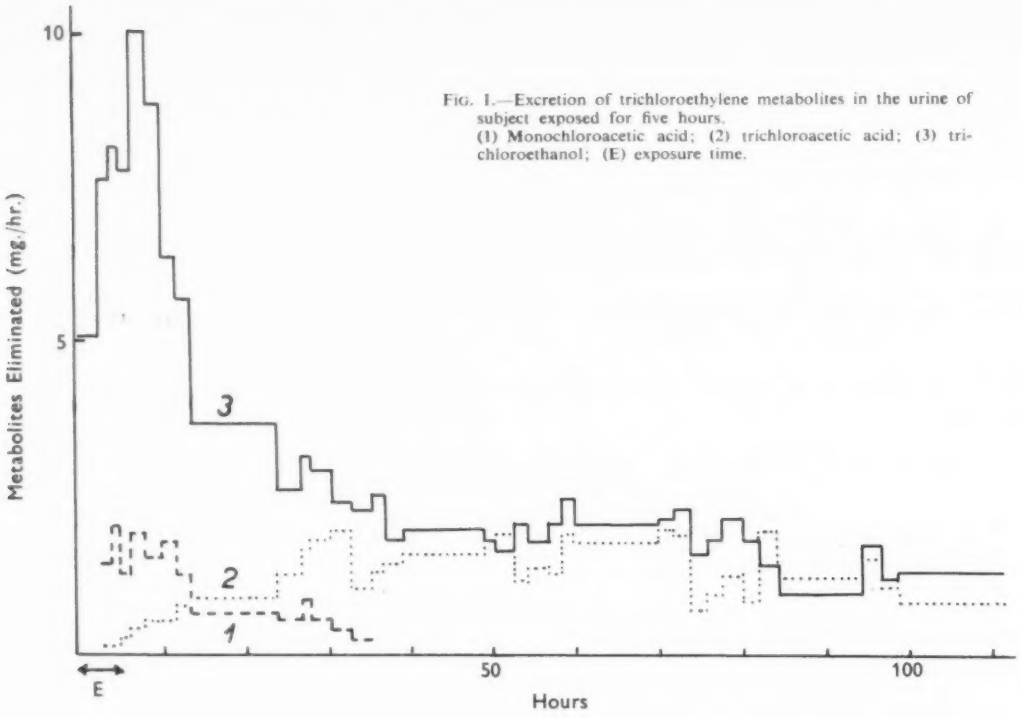


FIG. 1.—Excretion of trichloroethylene metabolites in the urine of subject exposed for five hours.
(1) Monochloroacetic acid; (2) trichloroacetic acid; (3) trichloroethanol; (E) exposure time.

within 24 hours in four experiments and within 48 hours in three others. After attaining the maximum, the fall in the rate of excretion could be analysed into the sum of two exponential rates.

The total quantity excreted was 120-560 mg. (average 260 mg.) representing 10-30% (average 19%) of the quantity of T.R.I. retained. Excretion lasted 312 to 520 hours (average 387 hours). The average half-period of excretion was 50 hours in the first phase, which lasted about five days, and 70 hours in the second phase, which lasted about 14 days.

The curve 2 in Fig. 1 shows the course of excretion of T.C.A. in one of the experiments, where the three metabolites were determined in each portion of urine excreted over a period of 110 hours from the termination of exposure. A feature of the excretion of T.C.A. is the periodicity; the amount in the urine reaches a maximum at 1300 hours each day, falls and rises again. These changes in the concentration of T.C.A. were not connected with the urine flow which varied only quite insignificantly.

Trichloroethanol.—This metabolite also appears in the urine very soon after the beginning of the inhalation of T.R.I. vapour. The quantity excreted rises rapidly, attaining its maximum a few hours after the end of exposure; its concentration then falls exponentially as the sum of two rates, a fast one at the beginning followed by a slower one.

The total quantity of T.C.E. excreted amounted to 415-655 mg. (average 520 mg.), representing 32-59% (average 50%) of the quantity of T.R.I. retained. The metabolite was excreted for 312 to 390 hours (average 350 hours). The average half-period of excretion was 24 hours in the first phase, which lasted three to four days, and 40 hours in the second phase, which lasted seven to nine days.

The concentration of T.C.E. in the individual urine specimens did not exhibit such a remarkable fluctuation in the course of the day as the concentration of T.C.A. (Fig. 1, curve 3).

The total quantity of all three metabolites excreted in the urine amounted to 43-101% (average 73%) of T.R.I. retained in the organism. The individual metabolites representing M.C.A. 4%, T.C.A. 19% and T.C.E. 50% give a ratio of approximately M.C.A. : T.C.A. : T.C.E. = 1 : 5 : 12.

In one experiment, glucose administered with insulin exerted a distinct influence on the total quantities of the three metabolites excreted. One man was exposed for five hours to T.R.I. concentrations of 500 and 530μg./l., respectively; the quantities of T.R.I. retained amounted to 770 and 860 mg. respectively and the percentage of each metabolite excreted was as follows:

Experiment		M.C.A. (%)	T.C.A. (%)	T.C.E. (%)
1	T.R.I. alone	5	30	45
2	T.R.I. followed by glucose and insulin	6	37	55

The giving of glucose and insulin caused an overall increase of approximately 22% for all metabolites excreted. On the first day after exposure the quantity of T.C.E. excreted was 2·6 times that excreted on the first day after exposure to T.R.I. alone. The quantity of T.C.A. was not noticeably influenced on the first day of excretion nor was the total duration of excretion of the metabolites influenced by the administration of glucose with insulin.

Discussion

The quantity of T.C.A. excreted after exposure of our subjects to T.R.I. vapours is in agreement with the findings in our earlier work and with those of other authors mentioned in the introduction. Considerable individual fluctuations in the quantities of this metabolite excreted were again confirmed. The causes of the periodic fluctuations of the T.C.A. concentration in the individual specimen of urine passed in the course of the day cannot be explained but show the inappropriateness of judging the level of exposure to T.R.I. from the quantity of T.C.A. found in an arbitrary sample of urine. For this purpose it is always necessary to analyse the total urine excreted during 24 hours in order to obtain significant results.

These experiments have again confirmed that the total quantity of T.C.E. excreted by man is approximately double that of T.C.A. This ratio applies to the total quantity of both metabolites excreted after a given exposure to vapours of T.R.I. This ratio, however, cannot be judged from the quantities found in single arbitrary samples of urine.

Monochloroacetic acid is only formed in quantities much lower than those of T.C.A. and T.C.E. Since M.C.A., however, is unquestionably the most toxic of the metabolites hitherto investigated, a certain significance could be ascribed to it in the overall toxicity of T.R.I.

According to Marhold (1953), the L.D.50 of some metabolites of T.R.I. for white mice when compared with that of sodium acetate are as follows:

	L.D.50 (g./kg.)
Sodium monochloroacetate	0·109 ± 0·050
Trichloroethanol	0·201 ± 0·012
Sodium acetate	0·404 ± 0·015
Sodium trichloroacetate	2·37 ± 0·11

The excretion of monochloroacetic acid from the organism proceeds fastest, that of trichloroethanol more slowly, and that of trichloroacetic acid is slower still. The half-periods of excretion (in hours) are approximately as follows:

	M.C.A.	T.C.E.	T.C.A.
First phase	15	24	50
Second phase	—	40	70

These rates of excretion seem to be comparatively constant. The slow excretion of T.C.A. is generally known for both man and various animals. The average excretion time of T.C.E. has been found to be 24 hours (20 to 29 hours). The data of Přerovská, Srbová, and Stýblová (1958), who investigated the excretion of T.C.E. after administration of T.R.I. by mouth, suggests a half-period of 28 hours; Bartoníček and Souček (1959), experimenting on rabbits, found an average half-period of 20 hours (14 to 26 hours).

Excretion and formation of T.R.I. metabolites can be influenced by drugs. According to Forssman, Owe-Larsson, and Skog (1955), the excretion of T.C.A., after giving T.R.I. to dogs and rats, drops practically to zero after administration of tetraethylthiuram disulphide (T.E.T.D.—"antabuse"). It is known that T.E.T.D. inhibits the oxidation to acetic acid of acetaldehyde in the organism. The finding of Forssman *et al.* could therefore be explained by assuming an inhibition of oxidation processes by which T.C.A. is formed from one of its possible precursors such as trichloroethanol or chloral, which in turn are formed in the organism from T.R.I. Administration of glucose with insulin, on the other hand, increases the quantity of excreted metabolites and thus influences the metabolism of T.R.I. in a positive sense. These findings could perhaps be utilized to influence the toxicity of T.R.I. or to influence the course of poisoning by this substance. Further research must decide whether inhibition or acceleration of the oxidation of T.R.I. or of its metabolites would be better suited for this purpose.

References

Ahlmark, A., and Forssman, S. (1949). Proc. IX. Int. Congr. Industr. Med., London, 1948, p. 552.

——, —— (1951). *Acta physiol. scand.*, **22**, 326.

Bardoděj, Z., and Krivucová, M. (1958). *Čsl. Hyg.*, **3**, 268.

Barrett, H. M., and Johnston, J. H. (1939). *J. biol. Chem.*, **127**, 765.

——, Cunningham, J. C., and Johnston, J. H. (1939). *J. industr. Hyg.*, **21**, 479.

Bartoníček, V., and Souček, B. (1959). *Arch. Gewerbepath. Gewerbehyg.*, **17**, 283.

Butler, T. C. (1949). *J. Pharm. exp. Ther.*, **95**, 84.

Fabre, R. (1949). Proc. IX. Int. Congr. Industr. Med., London, 1948, p. 546.

——, and Truhaut, R. (1952). *Brit. J. industr. Med.*, **9**, 39.

Forssman, S. (1945). *Svenska Läk.-Tidn.*, **42**, 1964.

——, and Ahlmark, A. (1946). *Nord. Med.*, **30**, 1033.

Forssman, S. and Holmquist, C. E. (1953). *Acta. pharmacol. (Kbh.)* **9**,235.
——, Owe-Larsson, A., and Skog, E. (1955). *Arch. Gewerbepath. Gewerbehyg.*, **13**, 619.
Grandjean, E., Münchinger, R., Turrian, V., Haas, P. A., Knoepfel, H. K., and Rosenmund, H. (1955). *Brit. J. industr. Med.*, **12**, 131.
Judah, J. D. (1949). *Biochem. J.*, **45**, 60.
Marhold, J. (1953). Laborat. zpráva VUOS, Pardubice-Rybitví.
Powell, J. F. (1945). *Brit. J. industr. Med.*, **2**, 142.
Přerovská, I. Srbová J., and Stýblová, V. (1958). *Pracov. Lék.*, **10**, 417.
Souček, B. (1954). *Ibid.*, **6**, 277.
—— (1955). *Ibid.*, **7**, 89.
——, and Pavelková, E. (1953). *Ibid.*, **5**, 62.
——, and Vlachová, D. (1954). *Ibid.*, **6**, 330.
——, Teisinger, J., and Pavelková, E. (1952). *Ibid.*, **4**, 31.
Teisinger, J., Stýblová, V., and Vlachová, D. (1955). *Ibid.*, **7**, 258.
Vlachová, D. (1955). *Ibid.*, **7**, 98.
—— (1957). *J. Hyg. Epid. Microbiol. Immunol.*, **1**, 225.

THE OCTOBER (1959) ISSUE

The October (1959) issue contains the following papers:—

Population Studies of Chronic Respiratory Disease: A Comparison of Miners, Foundryworkers, and Others in Staveley, Derbyshire. By I. T. T. Higgins, A. L. Cochrane, J. C. Gilson, and C. H. Wood.

Sickness Absence Among Railway Clerical Staff. By Derek S. Pugh, Cecil Gordon, and Katherine Lévy.

Pneumoconiosis in Carbon Electrode Makers. By A. J. Watson, J. Black, A. T. Doig, and G. Nagelschmidt.

The Effect of Different Concentrations of Silicic Acid and Silica Dust on the Biosynthesis of Collagen in Tissue Cultures. By M. Chvapil and D. Holečková.

Studies on the Nature and Aetiology of Respiratory Disability in Witwatersrand Gold-miners Free of Radiological Silicosis. By Margaret R. Becklake, Saul Zwi, and W. Lutz.

An Analysis of Some Observations of Thermal Comfort in an Equatorial Climate. By C. G. Webb.

Late Consequences of the Neurological Forms of Decompression Sickness. By I. Rózsahegyi.

Lung Cancer in Coal-miners. By R. Abbey Smith.

The Origin of the Term Anthracosis. By A. Meiklejohn.

Miscellanea:

A Laboratory Trial of Some Modern Screening Tests for the Detection of Glucose and Protein in Urine. By L. H. Turnbull.

Obituaries:

Mr. A. Treve Holman.
Dr. Lasar Dunner.

Book Reviews.

Index to Volume 16.

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, W.C.1, price 17*s.* 6*d.*

Brit. J. industr. Med., 1960, **17**, 65.

ECOLOGICAL CONSIDERATIONS ON NICKEL DERMATITIS

BY

POUL V. MARCUSSEN

From the Department of Dermatology, the Finsen Institute, Copenhagen, Denmark

(RECEIVED FOR PUBLICATION MARCH 6, 1959)

The incidence of nickel dermatoses has shifted from the plating industry to other occupations and particularly to non-occupational causes. A Danish survey of 621 cases shows that 4% are due to nickel plating, 9·5% to other occupations, and 86·5% were not due to occupation. A primary eruption not due to occupation had occurred in 14% of the occupational cases.

The importance of preventive measures for the community more than for the adequately controlled industry is underlined.

In 1954, Banks advanced the hypothesis that industrial premises had become safer places of work than the home where industrial products are used without guidance concerning their dangers. Moreover, individual tradesmen and artisans, using certain potentially hazardous substances without safeguards, may be sensitized before entering employment in factories. Nickel dermatitis, a case in point, is found both in factory workers and in the general population.

Previous Distribution of Nickel Dermatitis

Until 1930 many cases of skin disease in nickel platers were reported from most of the large industrial centres, for example, Berlin (Blaschko, 1889), Kiel (Schittenhelm and Stockinger, 1925), Leningrad (Kolzoff, 1926), Toronto, Ontario (Bulmer and Mackenzie, 1926), Oslo (Grön, 1929), and Geneva (Du Bois, 1931). The clinical picture of the disease agreed in the main with Blaschko's description of 1889, and often 50 to 100% of the workers seemed to be affected (Kolzoff, 1926; Schittenhelm and Stockinger, 1925; Wedroff, 1935). The disease was observed to relapse (Bulmer and Mackenzie, 1926; Grön, 1929; Schittenhelm and Stockinger, 1925) and chiefly to attack workers occupied directly with the nickel baths. In some instances the picture was complicated by corrosions and pyodermia, and as the concept of allergy was then unknown as a potential industrial hazard these phenomena were often believed to result from the actions of acid or alkali and high temperature (Bulmer and Mackenzie, 1926; Girard and Thévenard, 1923; Kolzoff, 1926). Schittenhelm and Stockinger in 1925 performed the first patch tests with nickel sulphate, but their results were criticized by Jadassohn and Schaaf in 1929 on the basis of workmen's compensation cases in Swiss industries. However, Wedroff in 1935 showed that nearly all the cases diagnosed in Moscow presented positive patch tests. Lahiri's (1957) and Lahiri and Barat's (1957) investigations in India gave similar results.

Wedroff (1935) pointed out that mechanization of the processes had rendered cases rare in factories and that single cases among self-employed artisans occurred more frequently than in factory workers. The varying standards of hygiene found in the workplaces considered may account for the contradictory observations during this period.

During the years 1930-40, when great hygienic reforms were introduced in industry, in part on an international scale, cases in workmen employed in factories seemed to disappear completely, but there were still reports of a number of carefully verified sporadic cases in industrial workers in large-scale industries (Assnin, 1933; Feit, 1930; Foster and Ball, 1935; Fuhs, 1927; Gerstein, 1927; Goldman, 1933; Gougerot, Barthélemy, and Arnaudet, 1930; Johnson, 1941; Lewith, 1928; Nékám, 1938; Riehl, 1932). The cases mentioned by Feit (1930), namely, of sensitization by nickel plating and subsequent eruption when the patient was working in a jeweller's shop, and by Johnson (1941) of a patient's sensitization by spectacle frames and eruption during work in a bicycle factory, are of special interest in relation to the present study. In 1936, Franck detected numerous cases in the

watch-making industry, the first described outside the nickel-plating industry.

Within the same period (1930-35) observations of nickel dermatitis produced by articles in everyday use were first reported. Rothman (1930), and Preininger (1934) reported it as due to coins, Lain (1931) and McAlester and McAlester (1931) to spectacle frames, Du Bois (1932) to a wrist watch, and Fox (1933) to a spectacle frame and wrist watch. Instances have since been described of sensitivity to almost any object that is nickel plated or contains a nickel alloy.

In 1939, Bonnevie, through systematic studies, demonstrated that nickel dermatitis was no rare phenomenon, constituting 5·2% of all contact dermatoses. He gave various examples from industries and trades. Skog and Thyresson (1953) found a preponderance of cases among building workers as well as in assistants in shops, stores, and offices. Finally, Calnan (1956) demonstrated that nickel dermatitis had become very frequent, a view borne out by other investigators (Fisher and Shapiro, 1956; Lahiri, 1957). Between 1936 and 1955 nickel dermatitis rose from 7·2 to 12·9% of verified sensitivities coincident with increasing imports of nickel (Marcussen, 1959). In this period the first descriptions were published of sensitivity to articles in everyday use, and from 1940 nickel dermatitis was observed to be somewhat common in the general population. From 1936, the different occupations in which workers are exposed to nickel can be traced in our records. The incidence of nickel dermatitis was found to have risen considerably during the past 20 years parallel with the increased use of the metal in everyday articles.

In the textbooks there are few comments on this problem. Mayer (1930), Blumenthal and Jaffé (1933), and Schwartz and Tulipan (1939) still regarded the existence of nickel dermatitis as doubtful or did not mention it. Schwartz, Tulipan, and Peck (1947) stated, in agreement with Wedroff (1935), that "Dermatitis . . . is common in small electroplating establishments where proper safety precautions are usually not as rigidly observed as in the large plants."

Recent Distribution of Nickel Dermatitis

The recent distribution of nickel dermatitis in the community has been studied on the basis of 621 verified* cases diagnosed during the years 1936-55 in the Department of Dermatology of the Finsen Institute. The technique of examination remained unaltered throughout this period. As nickel dermatitis is not recognized as an occupational disease in Denmark (Danish Workmen's Compensation Act, 1949) the investigation of compensation cases cannot have influenced the composition of the series. Of 621 patients, only 24 were shown to have been sensitized in the nickel-plating industry. This group constituted only 4% of the total series, whereas the remaining 96% had been sensitized by articles containing or covered by metallic nickel. It was, however, our impression that a much larger proportion of patients had dermatoses caused or aggravated by their occupation. All patients with dermatitis of the hands were sorted out (272 or 43·8%), and classified in 12 groups (Table 1). The remaining patients were thereafter assigned to the same groups and the percentages of dermatitis of the hands calculated. In Table 1 it is seen that in certain occupations a disproportionately large number of patients with dermatitis of the hands were found. Men in these occupations can therefore probably be regarded as particularly exposed. As expected, the groups accord largely with the examples of nickel dermatitis quoted by Bonnevie (1939), but differ essentially from the groups affected by detergents. All groups contain instances of sensitization by articles required for various occupations, *e.g.*, typewriters. Dermatitis of the hands was by no means always the primary eruption. The patients often exhibited a primary eruption provoked by articles used in the course of everyday life. Dermatitis of the hands was primary in only 114 cases (18·4%), while in 158 cases (25·4%) it occurred after sensitization

TABLE 1
CLASSIFICATION OF CASES

Occupation	Number of Patients	Number with Dermatitis of the Hands
Hairdressers	12	12 (100%)
Nickel platers	25	24 (96%)
Restaurant workers (including kitchen staff)	18	16 (88·9%)
The metal industries (including all work with tools and machines)	54	47 (87%)
Sewers, tailors	36	30 (83·3%)
Nurses, doctors, dentists	12	9 (75%)
Cashiers	14	10 (71·4%)
Shop assistants (especially chocolate and articles of food)	21	15 (71·4%)
Greatly exposed occupations (30·9%)	192	163 (84·9%)
Cleaning	30	9 (30%)
Office	40	12 (30%)
All other occupations and no occupation	38	10 (26·3%)
Housewives	321	78 (24·3%)
Less exposed occupations (69·1%)	429	109 (25·4%)
Total number	621	272 (100%)

*Verified nickel dermatitis is defined as dermatitis with a typical distribution and a positive patch test to 5% nickel sulphate.

TABLE 2
RATIOS OF PRIMARY AND SECONDARY DERMATITIS

	Number of Patients	Dermatitis of the Hands		
		Total	Primary	Secondary
Exposed occupations	192	163	75 (39·1%)	88 (45·8%)
Others	429	109	39 (9·1%)	70 (16·3%)
	621	272	114 (18·4%)	158 (25·4%)

elsewhere on the skin. This ratio was noticed in occupational as well as in non-occupational groups (Table 2).

Fig. 1 illustrates for the occupational groups the relative importance of various types of nickel-containing objects in presensitization. Women, owing to contact with nickel-containing objects in their clothing (especially suspenders), thus have a considerably greater chance of subsequently developing nickel dermatitis of the hands in certain occupations (Fig. 2).

The proposal to abolish nickel suspenders advanced by Wells (1956) is therefore well founded. Table 5 gives a survey of the aetiology of the primary eruption.

The present study (1936-55) thus showed that only 4% of patients had been sensitized in the nickel-plating industry,* 9·5% had been sensitized in other occupations, and 86·5% sensitized unconnected with their occupation. Of the last, not less than 14% of the total were later exposed occupationally to nickel and developed dermatitis of the hands. A greater number thus had a primary nickel eruption before entering an occupation entailing exposure to nickel.

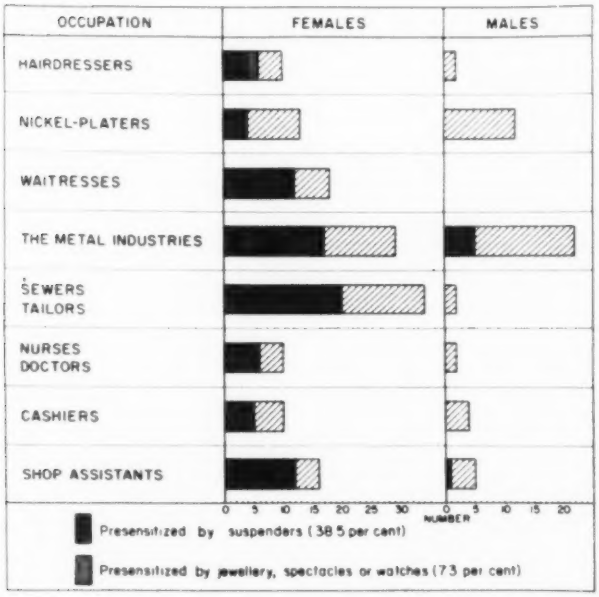


FIG. 1.—Nickel dermatitis in the greatly exposed occupations, showing the importance of presensitization.

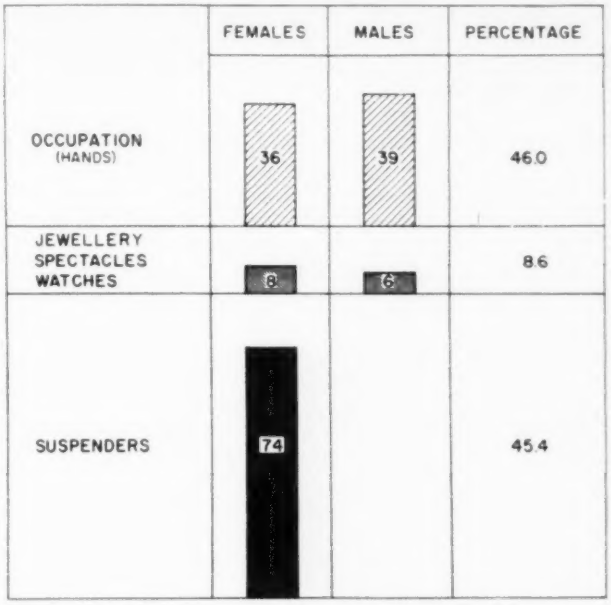


FIG. 2.—The aetiology of nickel dermatitis of the hands in the exposed occupations. Presensitization by nickel-plated suspenders is responsible for 45% of the cases of occupational dermatitis of the hands.

TABLE 3
SOURCE OF SENSITIZATION

Sensitized in	Number
Nickel-plating industries	24 (4%)
Other occupations	59 (9·5%)
Not employed	538 (86·5%)
Total	621 (100%)

Discussion

Published work on nickel dermatitis shows that accumulated cases in the large industries were common until 1930, but single cases not of occupational origin were not published. In the following years the disease largely disappeared from the large industries owing to improved hygiene in the work-

*A considerable error in the argument would arise if numerous cases occurred in the industry but were referred to other clinics. This is not the case. The Director of the Clinic of Occupational Diseases (Frost, personal communication) has informed us that 12 cases of nickel dermatitis were recorded during the period 1948-55, and that the Workmen's Compensation Board have registered three. Of these 15 cases, nine are included in the series under review.

shops, but in the same period an increasing number of cases were reported not originating occupationally in minor industries and among tradesmen and artisans.

Of the total number of cases of nickel dermatitis seen at the Finsen Institute during the period 1936 to 1955, only 4% could be referred to work with plating, while in 9·5% it had developed in other occupations and in 86·5% it was caused by articles in everyday use. Cases reported from the nickel industry were most infrequent during this period. Thus the results of the present study support the hypothesis that the risk of sensitization has moved from the adequately controlled industry to the uncontrolled private use of industrial products. Further, it has been found that 14% of the nickel-sensitive occupational cases have been presensitized in private life and consequently handicapped in future occupations involving the use of nickel. Our prophylactic efforts should possibly consist of informing the community as a whole of the direct hazards of dermatoses from the use of nickel and preventing those presensitized from work involving exposure to nickel. Nickel-plated suspenders should be replaced by nylon suspenders.

References

Assnin, D. (1933). *Arch. Dermat. Syph. (Berl.)*, **169**, 451.
Banks, A. L. (1954). In R. M. B. MacKenna *Modern Trends in Dermatology* (Second Series), p. 6. Butterworth, London.
Blaschko, A. (1889). *Disch. med. Wschr.*, **15**, 925.
Blumenthal, F., and Jaffé, K. (1933). *Ekzem und Idiosynkrasie*. Karger, Berlin.
Bonnevie, P. (1939). *Aetiologie und Pathogenese der Ekzemkrankheiten*. Busck, Copenhagen, and Barth, Leipzig.
Bulmer, F. M. R., and Mackenzie, E. A. (1926). *J. industr. Hyg.*, **8**, 517.
Calnan, C. D. (1956). *Brit. J. Dermat.*, **68**, 229.
Danish Workmen's Compensation Act No. 176 (April 12, 1949).
Du Bois, C. (1931). *Schweiz. med. Wschr.*, **12**, 278.
—— (1932). *Ann. Derm. Syph. (Paris)*, VII sér. **3**, 209.
Feit, H. (1930). *Arch. Derm. Syph. (Chicago)*, **21**, 481.
Fisher, A. A., and Shapiro, A. (1956). *J. Amer. med. Ass.*, **161**, 717.
Foster, P. D., and Ball, F. I. (1935). *Arch. Derm. Syph. (Chicago)*, **31**, 461.
Fox, H. (1933). *J. Amer. med. Ass.*, **101**, 1066.
Franck, G. (1936). *Schweiz. med. Wschr.*, **17**, 232.
Fuhs, H. (1927). *Zbl. Haut.-u. Geschl.-Kr.*, **24**, 750.
Gerstein, H. (1927). *Ibid.*, **23**, 163.
Girard, L., and Thévenard, S. (1923). *Bull. Soc. méd. Hôp. Paris*, 3 ser., **47**, 1612.
Goldman, L. (1933). *Arch. Derm. Syph. (Chicago)*, **28**, 688.
Gougerot, Barthélemy, and Arnaudet (1930). *Bull. Soc. franç. derm. syph.*, **37**, 117.
Grön, K. (1929). *Urol. cutan. Rev.*, **33**, 606.
Jadassohn, W., and Schaaf, F. (1929). *Arch. Derm. Syph. (Berl.)*, **157**, 572.
Johnson, H. H., Jr. (1941). *Arch. Derm. Syph. (Chicago)*, **43**, 575.
Kolzoff, H. (1926). *Zbl. Gew.-Hyg.*, n.s., **3**, 339.
Lahiri, K. D. (1957). *Indian J. Derm.*, **2**, 110.
——, and Barat, D. B. (1957). *Ibid.*, **2**, 77.
Lain, E. S. (1931). *J. Amer. med Ass.*, **96**, 771.
Lewith, R. (1928). *Zbl. Haut.u. Geschl.-Kr.*, **26**, 348.
McAlester, A. W. Jr., and McAlester, A. W., Third (1931). *Amer. J. Ophthal.*, **14**, 925.
Marcussen, P. V. (1959). *Brit. J. Derm.*, **71**, 97.
Mayer, R. L. (1930). *Das Gewerbeekzem*. Springer, Berlin.
Nékám, L. Jr. (1938). *Zbl. Haut.-u. Geschl.-Kr.*, **59**, 244.
Preininger, T. (1934). *Derm. Wschr.*, **99**, 1082.
Riehl, J. (1932). *Zbl. Haut-u. Geschl.-Kr.*, **41**, 294.
Rothman, S. (1930). *Derm. Wschr.*, **90**, 98.
Schittenhelm, A., and Stockinger, W. (1925). *Z. ges. exp. Med.*, **45**, 58.
Schwartz, L., and Tulipan, L. (1939). *Occupational Diseases of the Skin*. Lea and Febiger, Philadelphia.
——, ——, and Peck, S. M. (1947). *Ibid.*, 2nd edition.
Skog, E., and Thyresson, N. (1953). *Acta derm.-venereol (Stockh.)*, **33**, 65.
Stewart, S. G. (1933). *Arch. intern. Med.*, **51**, 427.
Wedroff, N. (1935). *Arch. Gewerbepath. Gewerbehyg.*, **6**, 179.
Wells, G. C. (1956). *Brit. J. Derm.*, **68**, 237.

Brit. J. industr. Med., 1960, **17**, 69.

RENAL LESIONS IN EXPERIMENTAL CADMIUM POISONING

BY

J. A. BONNELL, J. H. ROSS, and E. KING

From the Department for Research in Industrial Medicine, Medical Research Council, The London Hospital

(RECEIVED FOR PUBLICATION MARCH 12, 1959)

A series of controlled experiments was carried out on rats to study the effects on the kidneys of the repeated administration of small doses of cadmium for periods of up to 12 months. Renal lesions consisting essentially of tubular atrophy and interstitial fibrosis were produced, and the evidence that these lesions were due solely to cadmium is discussed. No similar lesions occurred in a series of control animals, litter mates of the experimental animals. The lesions were shown to be reproducible in two prolonged experiments on two strains of rats. The relationship between the lesions and the concentration of cadmium in the tissues of the rats is discussed and a comparison is made with tissues from human cases of chronic cadmium poisoning. It is of interest that the cadmium concentration of human tissues and rat experimental tissue is of the same order of magnitude. Animals in which the administration of cadmium was discontinued after five months of the experiment had developed as severe lesions seven months later as those animals which had received cadmium for 12 months. It has been shown previously that the first sign of chronic cadmium poisoning can occur in man for the first time many years after the last exposure, and that the disease once established in man is progressive despite the absence of further exposure.

Emphysema and proteinuria have been described in men exposed to cadmium oxide as either dust or freshly formed fume (Friberg, 1948; Bonnell, 1955). The significance of the proteinuria and its relationship to progressive renal damage has been discussed by Bonnell, Kazantzis, and King (1959).

Because the evidence that progressive renal damage occurred in men suffering from chronic cadmium poisoning was incomplete, experiments were carried out to study the effect of repeated small doses of cadmium on the kidneys of rats. These experiments are described here, together with a review of the literature involving animal experiments with cadmium.

Review of the Literature

The earliest work on the toxic effects of cadmium in animals was published by Marmé in 1867. He determined the lethal dose of 14 cadmium compounds on dogs, cats, rabbits, and pigeons. The cadmium was administered intravenously, subcutaneously, and orally. He found that the lethal dose for dogs was 30 mg. intravenously and 60-90 mg. subcutaneously. The lethal dose for rabbits was 300-600 mg. by mouth. Small doses of cadmium salts were found to produce chronic effects but the actual doses were not mentioned. At necropsy these animals were found to have infarction of the lungs with subpleural haemorrhages, fatty degeneration of the liver and heart, and a diffuse inflammation of the kidneys. The excretion of cadmium was found to be slow and to occur mainly in the urine.

The effect of cadmium on the kidneys was studied by Severi in 1896. Ten milligrammes of cadmium as a 1% solution of cadmium chloride were injected subcutaneously in rabbits and dogs first daily and then on alternate days. The macroscopic and microscopic appearances of the kidneys were said to resemble closely the kidneys in mercuric chloride poisoning. There was an intense necrosis of the convoluted tubules, the cells were poorly defined, pale and with irregular granulations. There were tubular casts which appeared to be formed from the desquamating cells, and some calcified casts.

Alsberg and Schwartze (1919), using cats, dogs, rabbits, and rats as experimental animals, reported renal changes after parenteral administration but no histological details were given. No other pathological changes were noticed and no cumulative effects were noted with small doses.

Johns, Finks, and Alsberg (1923) showed that the

growth of young rats was completely retarded by a diet containing 250 p.p.m. of cadmium. The initial growth rate was normal on diets containing 125 p.p.m. but all the male rats died within 56 days. Diets containing 62·5 p.p.m. produced no noticeable effects. Similar effects on growth were noted by Schwarz and Otto (1925) but they also reported a reduction in the haemoglobin content of the blood. Haemoglobin estimations in rats fed 1-11 mg./kg. of cadmium demonstrated a fall of 10 to 20% in the haemoglobin (Sahli scale).

Prodan (1932) devised a series of inhalation experiments on cats using cadmium fume, cadmium oxide, and cadmium sulphide. Two cats were exposed to a high concentration of cadmium fume for 30 minutes. One cat was killed five hours later and the other died 12 hours after exposure. Both had acute pneumonia. Three other cats were exposed for 24 hours to a lower concentration of cadmium fume (the settling curve showed an initial concentration of 16 mg./m.^{3} which fell to 4 mg./m.^{3} after 24 hours). All three cats developed acute pulmonary lesions. The first cat was killed immediately after exposure; the other two cats were killed five and nine days later. The lungs showed areas of acute inflammation, collapse, and acute emphysema. There were haemorrhages in the bronchioles and acute inflammatory changes in the liver and kidneys. Prodan estimated that the cats retained only 3 to 6 mg. of cadmium. In another experiment two cats were exposed to cadmium oxide dust at a concentration of 400 mg./m.^{3}. The necropsy findings were similar to those in the animals exposed to cadmium fume. Cats exposed to cadmium sulphide showed changes in the lungs similar to those seen in animals exposed to cadmium fume and cadmium oxide dust.

Wilson, DeEds, and Cox (1941) studied the effect of adding cadmium to the diet of rats. Male albino rats were fed on diets containing 0, 0·0031, 0·0062, 0·0125, 0·025, and 0·05% cadmium as cadmium chloride. Three effects were noticeable: (*a*) The effect on the growth of the animals; (*b*) the production of anaemia; and (*c*) the effects on the teeth. The growth of the animals was retarded in direct relation to the concentration of cadmium in the diet. The rats taking 0·0125% cadmium in the diet were markedly affected after 84 days. When their diet was replaced with a normal diet, they rapidly attained a normal rate of growth with no apparent ill effects. Feeding on a diet containing as little as 0·0031% cadmium produced an anaemia which was sufficiently severe to alter the normally pink eyes of the albino rats. When the diet contained 0·0062% cadmium the haemoglobin dropped from a normal 16·5% to 3 to 4% in three months. The most sensitive criterion of chronic absorption of cadmium discovered in this work was the effect on the teeth. The normally yellow incisor teeth were bleached by cadmium, the effect being almost identical with that produced by fluorine poisoning. Statistically significant increases in weight were found for the heart, adrenals, and kidneys of these animals at necropsy. The mean weight of the hearts of rats on a diet containing 0·0125% cadmium was almost double that of the control animals. Microscopic examination of the heart showed hypertrophy of the cardiac muscle, which was claimed to be due to the anaemia and not to renal damage. Histological examination of the other organs showed a subacute pancreatitis, particularly in the rats absorbing 0·025% cadmium. There were focal areas of centrilobular necrosis with lymphocytic infiltration in the liver. There was swelling and granulation of the epithelium of the convoluted tubules of the kidneys with formation of both hyaline and granular casts. All these effects were more marked in the rats taking a diet containing 0·025 and 0·05% cadmium.

Princi and Geever (1950) described experiments in which dogs were exposed to cadmium sulphide and cadmium oxide dusts in specially constructed tanks. The dogs were exposed to cadmium oxide dust for six hours daily for five days each week at a mean concentration of 4 mg./m.^{3}. Ninety-eight per cent. of the dust particles were less than 3μ in diameter and no particle greater than 5μ was seen. The dogs were exposed for periods which averaged 1,102 hours.

Complete necropsies on all 30 dogs showed no significant abnormalities. The lungs, liver, and kidneys were carefully examined, but even though appreciable quantities of cadmium were found in the organs, there were no structural changes. Blood cadmium levels varied between 0·3 μg./g. blood after one week and 2·2 μg./g. after 12 months' exposure. The cadmium excreted in the urine was *c.* 6 μg./litre after one week and *c.* 387 μg./litre after 12 months' exposure. The blood and urine cadmium levels after exposure to cadmium sulphide were much lower. The cadmium concentration in the liver and kidney was 20·6 to 133 μg./g. of kidney and 12·4 to 4·70 μg./g. of liver. Princi suggested as a result of these experiments that the maximum allowable concentration of cadmium in the atmosphere of workshops should be increased.

Friberg (1950a and b) described experiments in which rabbits were exposed to cadmium dust in two groups of 13 and 12 for seven and nine months respectively. The first group were exposed for seven months to dust of cadmium and iron (containing 20% of iron) at a concentration of 10 mg./m.^{3}.

They were exposed for three hours daily, six days a week. The second group were exposed to the same dust in the same way for nine months. The average concentration of the dust in the atmosphere was 7 mg./m.^{3}. Ninety-five per cent. of the dust particles were less than 5 μ in diameter and 55% were less than 1 μ.

The urine was tested periodically with 25% trichloracetic acid and 25% nitric acid. From the fourth month onward proteinuria was found, increasing in incidence with time. Twenty-two rabbits survived the experiment and of these nine had a constant proteinuria from the fourth month, six had proteinuria during half of the time tested, five had proteinuria on isolated occasions, and no proteinuria was demonstrated at any time in two. At necropsy, 16 showed a chronic inflammation of the nasal mucous membranes, 20 had chronic tracheitis, and all were found to have chronic bronchitis and emphysema. There was fatty infiltration of the liver and inflammatory foci were found in the kidneys of the majority. The kidneys contained 300-700 μg./g. of cadmium, the liver 100-400 μg./g., and the lungs 50-150 μg./g.

In a second experiment, 15 rabbits were injected subcutaneously with 0·3% solution of cadmium sulphate in water (1 ml. contained 3 mg. $CdSO_4 \equiv$ 1·3 mg. Cd). Each rabbit was given 0·5 ml./kg. of body weight once daily for six days each week. Six rabbits were killed after two months, five survived for six months and were killed, and four died during the course of the experiment. Proteinuria was demonstrated in all the animals after two months. The protein was shown to behave differently on physico-chemical examination from the protein produced in uranyl nephritis in rabbits. All the animals became progressively more anaemic.

At necropsy the livers were granular and of abnormally firm consistency. The spleens were enlarged, weighing five times as much as the spleens from control rabbits. Chronic inflammatory changes were present in the upper respiratory tract. The liver showed a pronounced periportal cirrhosis and there was a non-specific hyperplasia of the spleen. The kidneys showed chronic inflammatory changes with interstitial infiltration of lymphocytes as well as plasma cells. Hyaline casts were present in the tubules.

Dalhamn and Friberg (1957) in a later series of experiments described renal tubular necrosis in rabbits after 10 weeks' subcutaneous injection of cadmium sulphate as described above.

There are several conflicting reports of renal involvement in animals given cadmium either by mouth or parenterally. In none of the reports are detailed descriptions of renal histology given and for this reason the following experiments were carried out.

Method

Male and female albino rats of the Wistar strain, "Glaxo" and "Chester-Beatty" breeds, aged 3 months and weighing about 200 g., were used in the experiments. Cadmium was given by intraperitoneal injections as a solution of cadmium chloride in distilled water (1 ml. $\equiv$ 1 mg. Cd). At this dilution the solution was neutral. In all these experiments, the rats were killed at intervals by chloroform anaesthesia, necropsies were performed, and the livers and kidneys were examined histologically. Tissues were fixed in formol saline. Sections of 5μ thickness were cut and stained with haematoxylin and eosin and a connective tissue stain. In some cases frozen sections were cut and stained with Sudan III to show fat. In six cases at the end of the experiment cultures were made on blood agar and McConkey media from kidneys sectioned with sterile precautions. Urine was obtained from rats in experiments 2 and 3 by holding the animal over a petri dish and stimulating micturition by ether inhalation. The urine was collected in a pipette and the uncentrifuged deposit was examined microscopically.

Results

Experiment 1.—Six pairs of female rats were given single intraperitoneal injections of cadmium at a dose of 2·5, 3, 4, 5, 6, and 7 mg. Cd/kg. The rats given 6 and 7 mg./Cd./kg. died within 12 hours, of those given 4 and 5 mg. Cd./kg., three died within 12 hours and the other was killed four days later. The four remaining rats which received 2·5 and 3 mg. Cd/kg. were unaffected; two were killed 24 hours later, one after four days and one after three months. Necropsies were performed on all five animals killed and the liver and kidneys were examined histologically. No macroscopic or microscopic abnormalities were found in the liver and kidneys of these five rats. Frozen sections were not obtained. These doses of cadmium were not well tolerated and the animals appeared to suffer from an acute irritative peritoneal lesion. Animals killed or dead within 24 hours of the injection had an acute haemorrhagic peritonitis with a blood-stained effusion.

Experiment 2.—A pilot experiment to study the effect of repeated injections of cadmium was begun in January, 1955. Ten female and eight male rats, aged 12 weeks and weighing from 150 to 200 g. were given intraperitoneal injections of cadmium thrice weekly at a dose of 1 mg. Cd/kg. Two male rats were used as control animals and were given intraperitoneal injections of physiological saline. Microscopical examination of the urine was carried out on a number of rats each week. Single rats were killed each week from the sixth to the ninth,

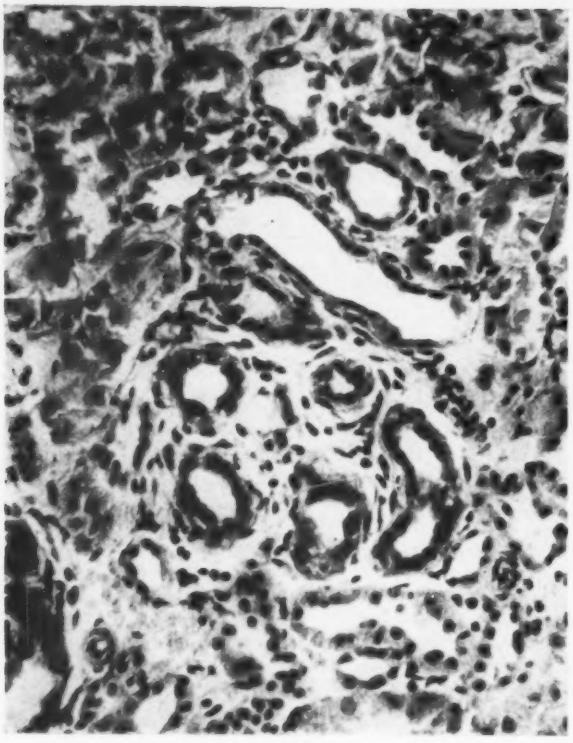


FIG. 1.—Rat 19, female, killed at eight weeks. Haematoxylin and eosin, × 300. Small area with dilated tubule, convoluted tubules with flattened basophil cells and surrounding interstitial reaction.

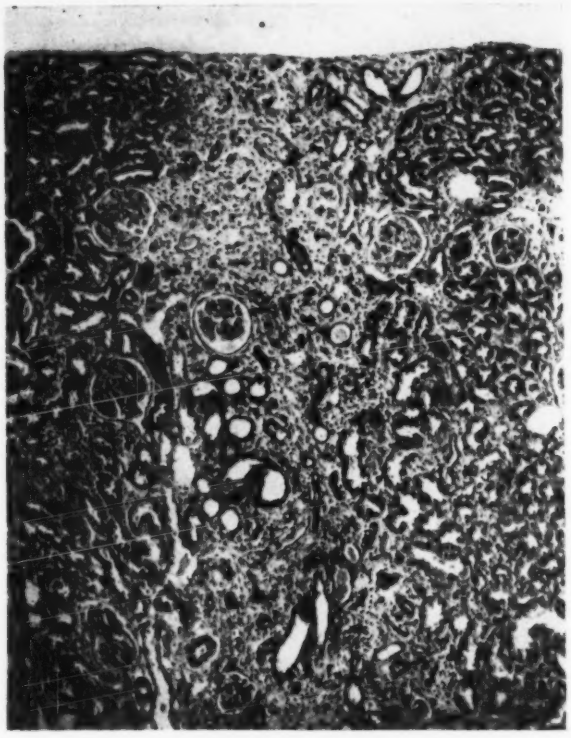


FIG. 2.—Rat 5, male, killed at 28 weeks. Haematoxylin and eosin, × 75. Subcapsular area with tubular atrophy and dilatation and increased interstitial tissue.

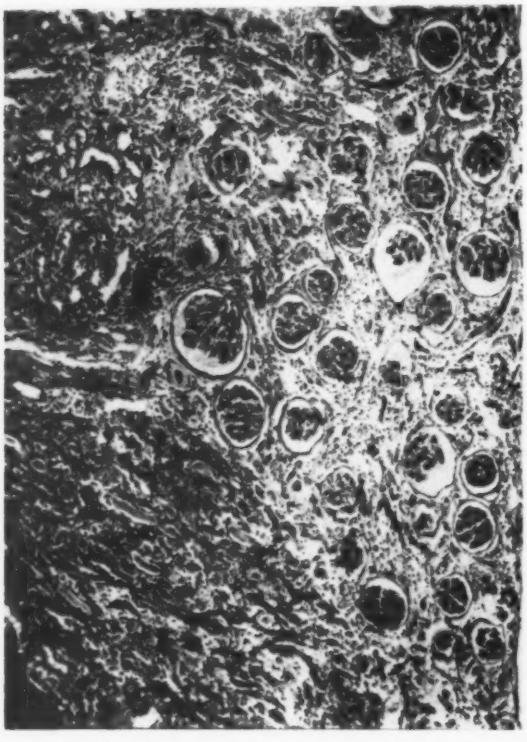


FIG. 3.—Rat 21, female, killed at 45 weeks. Haematoxylin and eosin, × 59. Cortex with marked tubular atrophy and crowding together of glomeruli, some of which have shrunken tufts and dilated capsular spaces.

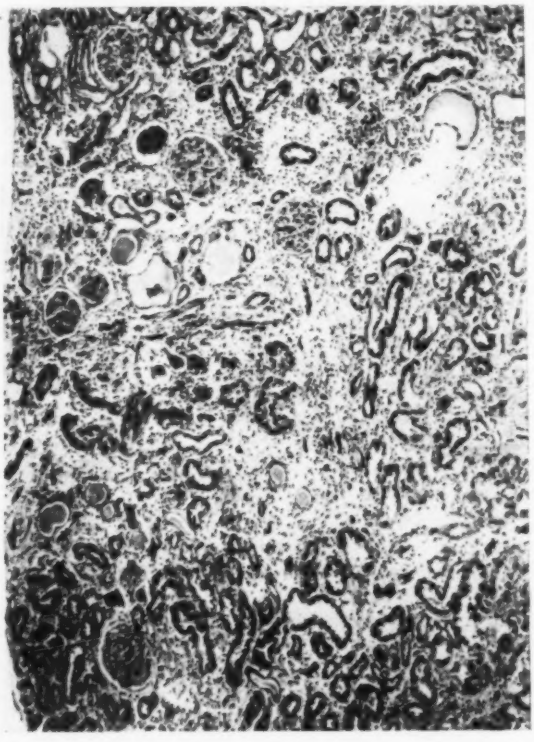


FIG. 4.—Rat 20, female, killed at 45 weeks. Haematoxylin and eosin, × 68. Cortex with tubular atrophy and occasional dilatation and increase in interstitial tissue.

14th-18th, and 23rd-29th weeks inclusive and the remainder at the 32nd and 45th weeks.

Urine Examination.—Excess red blood cells and granular and cellular casts were regularly found in the urine of all rats receiving intraperitoneal cadmium after one month.

Macroscopic Findings.—There was evidence of peritoneal reaction to the cadmium injections in all these rats. Free fluid was frequently found in the peritoneal cavity and the peritoneum covering most organs and lining the abdominal wall was irregularly thickened by fibrosis. The liver was distorted by fibrous bands replacing peritoneum in rats killed after three months (but microscopic examination showed no intrahepatic lesions). The heart and lungs appeared normal.

The kidneys of rats killed up to 24 weeks appeared normal on section. After 24 weeks blurring of the cortical pattern and corticomedullary junction was occasionally noted. The kidneys of one female rat killed at 32 weeks and of the two female rats killed at 45 weeks were contracted with finely granular surfaces, contracted blurred cortices, and absent or ill-defined corticomedullary demarcations.

Microscopic Findings.—The kidneys of rats killed at six, seven, eight, and nine weeks showed: (*a*) no abnormality (two rats), or (*b*) vacuolation with a slightly ragged appearance of the cells of the convoluted tubules (one rat), or (*c*) a few small areas in the cortex, usually subcapsular, containing dilated tubules with eosinophil cast material, slightly increased interstitial tissue and very slight interstitial lymphocytic infiltration. Flattened basophil tubular cells were considered to indicate regenerative activity (two rats) (Fig. 1).

The kidneys of rats killed from 14 to 45 weeks showed lesions as in (*c*) above, their severity increasing with the duration of the injections. The normal architecture of the kidneys was altered by irregular areas of tubular destruction. This consisted of tubular atrophy with tubular remnants lying within increased interstitial tissue containing a few chronic inflammatory cells (Fig. 2). Occasional tubules were dilated with flattened lining cells and contained eosinophil material. In the least involved specimens the affected areas were mostly subcapsular and approximately wedge-shaped with slight "dimpling" of the capsular surface; deeper in the cortex the areas were irregular. The glomeruli were normal, apart from some dilated capsular spaces and shrunken tufts in the most advanced specimens. Medullary tubules contained eosinophil casts and were occasionally surrounded with a few chronic inflammatory cells.

The lesions were most marked in the kidneys of rats killed after 32 weeks, in which the tubular destruction had led to cortical contraction and fibrosis with crowding together of the glomeruli (Figs. 3 and 4). Fat stains showed that the surviving convoluted tubules in some specimens contained many fat-filled vacuoles. Regenerative activity in some tubules was frequently noted.

The kidneys of two male rats given intraperitoneal saline for 23 and 28 weeks showed no abnormalities.

Experiment 3.—The pilot experiment demonstrated that renal lesions could be produced by cadmium injected intraperitoneally. In order to study this lesion in greater detail and to confirm that the results were reproducible a further experiment was started in January, 1956. In this experiment 35 male and 30 female rats were given cadmium by intraperitoneal injections at a dose of 0·75 mg. Cd/kg. thrice weekly. Twenty male and 20 female rats, litter mates of the experimental animals, were used as controls; these animals were given intraperitoneal injections of distilled water thrice weekly. Four experimental rats, two female and two male, together with two control rats, one female and one male, were killed each month. Necropsies were carried out on each animal, the liver and kidneys were examined histologically, and the cadmium content of all the tissues was determined by polarographic analysis. Since rats have a physiological proteinuria, no estimations of urinary proteins were carried out.

This experiment had to be modified slightly because after five months the male rats and after six months the female rats showed signs of severe debility and the injections were discontinued until the end of the seventh month. At this time nine male and nine female rats were given further injections of cadmium chloride, but at a reduced dose rate of 0·25 mg.Cd/kg. thrice weekly. The remaining five male and five female rats were not given any further doses of cadmium. The control rats continued to receive intraperitoneal injections of distilled water throughout the experiment.

At the end of the experiment the exposed animals consisted of a group of males which had been dosed for five months and left for a further seven and a group of female rats dosed for six months and left for six months, together with a group of males and a group of female rats which were given 0·75 mg. Cd/kg. for five and six months and then 0·25 mg. Cd/kg. from the seventh to the twelfth months.

Sections from the kidneys of 35 control rats and 59 rats injected with cadmium were available for histological study; five control rats and six cadmium-injected rats died and their kidneys were

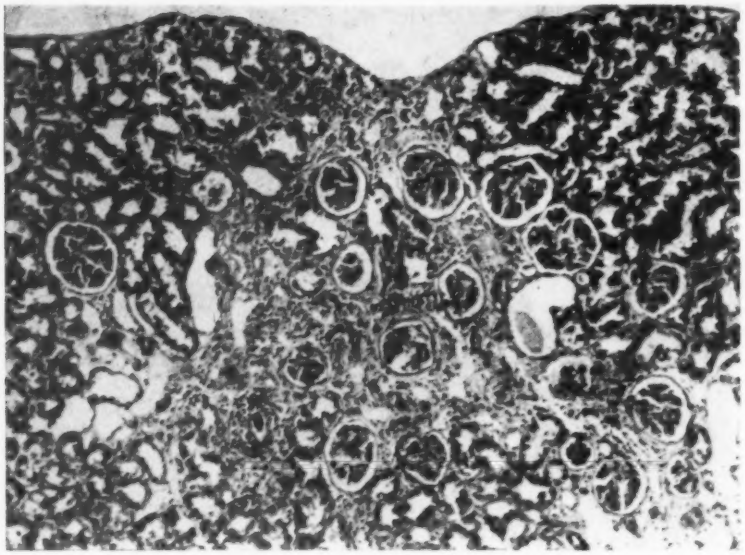


FIG. 5.—Rat 27, female, killed at twelve months. Haematoxylin and eosin, × 80. Cortical area of contraction with tubular atrophy and dilatation and crowding together of glomeruli.

too damaged for examination. In some of these cases the tissues were suitable for chemical analysis. On other occasions mishaps during the preparation of tissues made chemical analysis impossible.

The microscopic renal lesions observed were identical in nature to those found in experiment 2 but less severe; kidneys from rats killed at 45 weeks in experiment 2 showed more extensive lesions than those from rats killed at 52 weeks in this experiment (Fig. 5).

The lesions have been graded as follows:—

0—No abnormality other than occasional vacuolation within cells of convoluted tubules.

1—Very small areas with tubular atrophy, slightly dilated tubules containing casts and slight chronic inflammatory cell infiltration.

2—Many areas in cortex of tubular atrophy with associated features as in 1, and with increased interstitial tissue.

3—Cortex almost uniformly involved by lesions as in 2, with or without cortical contraction and crowding together of glomeruli.

Table 1 shows the numbers of rats at different periods with lesions of grades 0 to 3. Those rats which had obvious pyelonephritis with marked polymorphonuclear leucocyte and chronic inflammatory cell infiltration are indicated under a separate heading as is one rat which had an abscess in one kidney. The lesions were bilateral and of approximately equal severity in each kidney. No lesions were found before four months; they became more marked with longer durations (Fig. 6). Rats which were killed at nine and 12 months but had not been injected after six months had lesions of similar

TABLE 1

GRADING OF MICROSCOPIC LESIONS IN CADMIUM-INJECTED AND CONTROL RATS

Month	0		1		2		3		Pyelonephritis		Abscess Formation	
	Control	Cd	Control	Cd	Control	Cd	Control	Cd	Control	Cd	Control	Cd
1	1	6										
2	2	3								1		
3	2	4										
3½		1										
4	1	2		2					1			
5	1	2		3					1			
5½										1		1
6	2					3						
6½						1		1				
7	2			2		2						
7½				1		1		1		1		
8½	2		2			1		1				
9	1			2(2)†		2(1)			1			
12	15		1	2		6(2)		6(2)				

† Figures in brackets indicate numbers of rats, included in the adjoining total, which were not injected after six months.

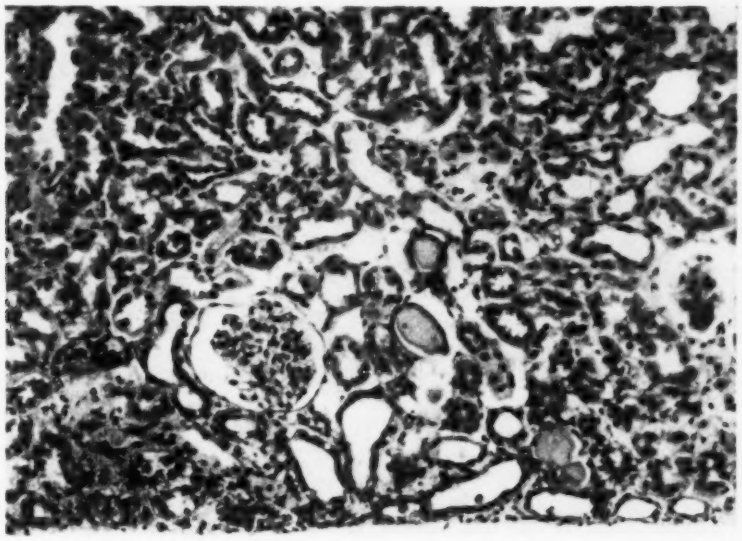


FIG. 6.—Rat 10, female, killed at four months. Haematoxylin and eison, × 150. Early subcapsular lesion.

intensity to those injected up to nine and 12 months.

The kidneys of three control rats had very small areas of tubular atrophy with surrounding small round cell infiltrations. These lesions were similar to those graded 1 in the cadmium-injected rats and have been graded as such, although, in one instance. the inflammatory cell infiltration was more marked.

Pyelonephritis was obviously present in some areas of the kidneys of one cadmium-injected rat killed at six months, which was graded 2 as elsewhere there were areas of tubular atrophy without marked interstitial inflammatory infiltration. In addition one cadmium-injected rat killed at 12 months had a few polymorphonuclear leucocyte tubular casts in addition to widespread tubular atrophy and distortion.

Within four to five months the central incisor teeth of the cadmium-injected rats became bleached

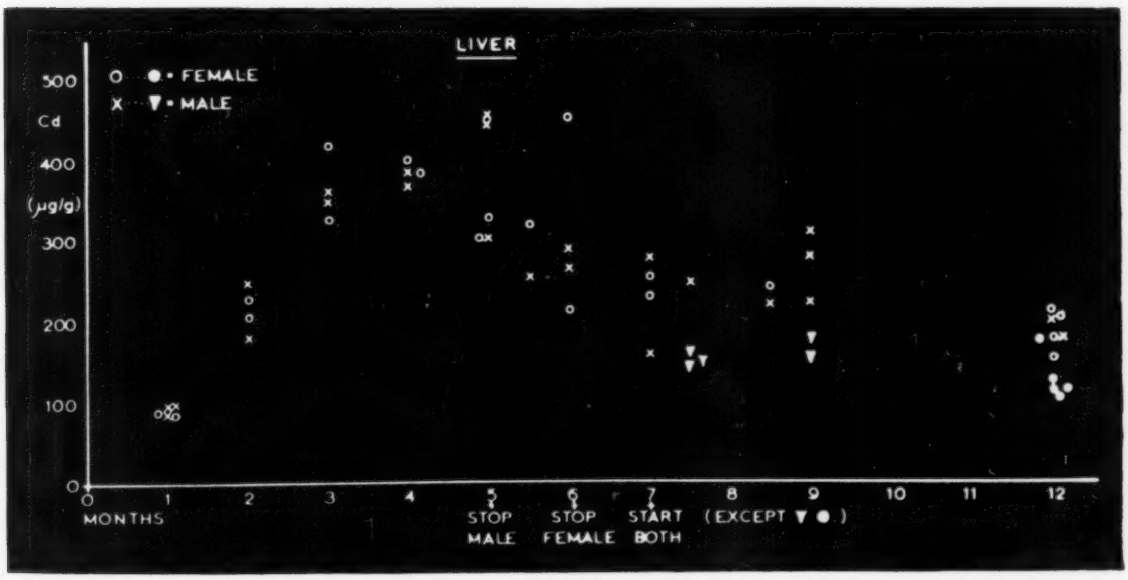


FIG. 7.—Tissue concentration of cadmium in the liver.

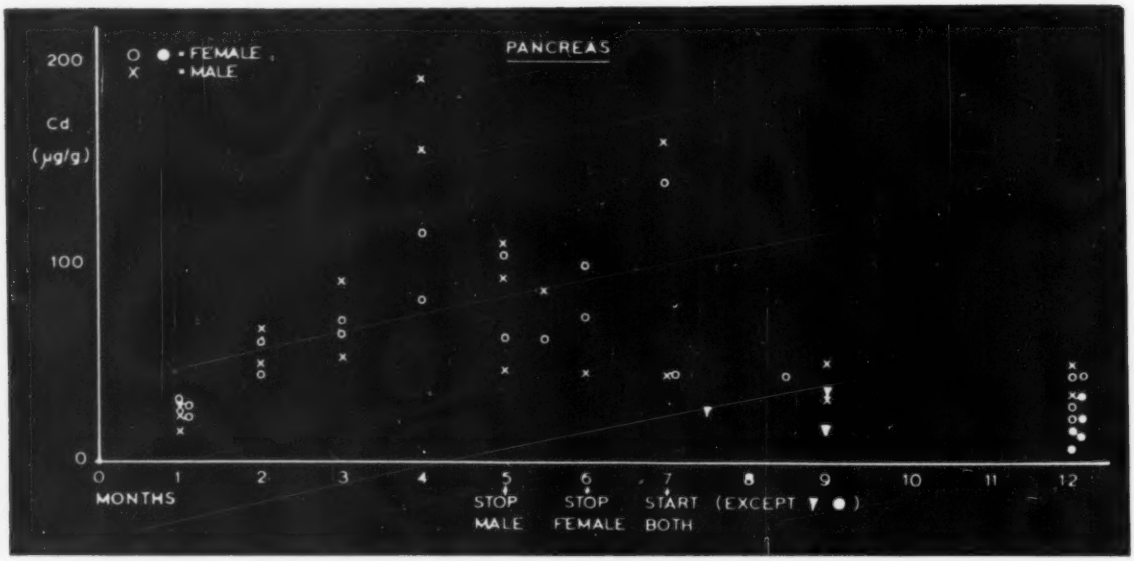


FIG. 8.—Tissue concentration of cadmium in the pancreas.

and appeared white compared with the normal orange-yellow colour of the teeth of the control rats. This bleaching of the teeth was permanent and confirms the findings of Wilson *et al.* (1941).

Tissue Concentration of Cadmium

The concentrations of cadmium in the liver, kidneys, spleen, and pancreas of the experimental animals are shown graphically in Figs. 7-10.

It can be seen from Fig. 7 that the liver concentrations of cadmium increased linearly up to the third month, when a plateau was reached. The concentration of cadmium then fell rapidly in the two months following cessation of the injections and then more gradually until the end of the experiment. The liver concentrations of those animals in which the injections were recommenced at the lower dosage did not attain their former high level.

The concentration of cadmium in the pancreas

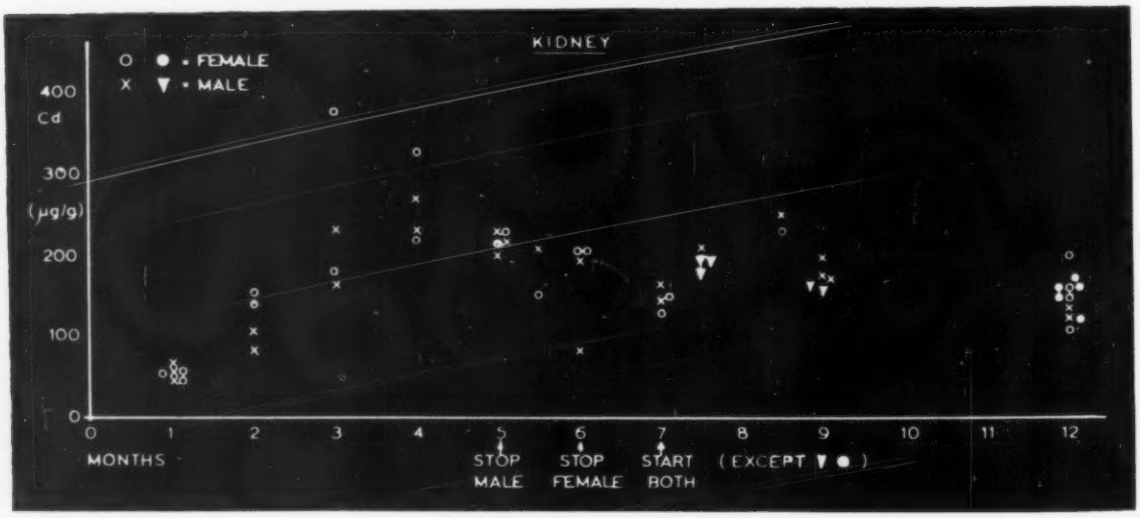


FIG. 9.—Tissue concentration of cadmium in the kidneys.

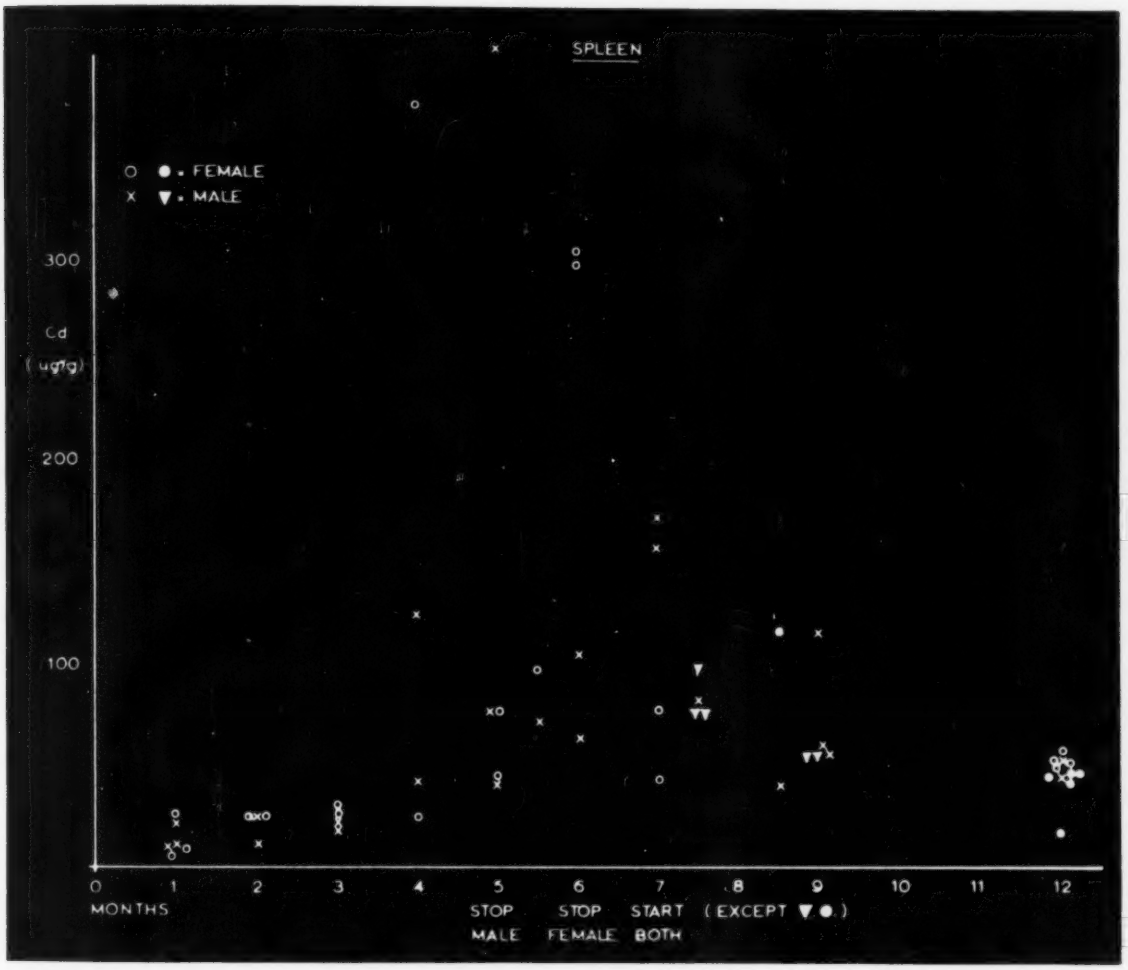


FIG. 10.—Tissue concentration of cadmium in the spleen.

closely paralleled that in the liver, but at a lower level (Fig. 8).

The cadmium concentration in the kidneys (Fig. 9) also increased linearly for the first three to four months after which a plateau was reached. It can be observed that there was little decrease in these levels after dosage had been stopped and that the further injections of small quantities of cadmium did not increase the levels above those of the animals which were not injected after six and seven months.

The spleen contained little cadmium until the fifth month when the concentration rose sharply to a very high level and then decreased rapidly on cessation of dosage (Fig. 10).

The blood cadmium levels were high during the fourth, fifth, and sixth months of the experiment, amounting to an average concentration of 10 μg. Cd/ml. blood. The cadmium was present in the red blood cells and not in the plasma, confirming the findings of Friberg (1952). The high splenic cadmium concentration occurred one to two months after the high blood levels were first observed, suggesting that they were connected with the destruction of circulating red blood cells. By the end of the experiment the blood cadmium concentrations were insignificant. Other tissues examined were voluntary muscle, heart muscle and involuntary muscle, lungs, skin, long bones, sternum and vertebrae (with and without marrow), teeth and jaw, brain, salivary glands, thyroid, adrenals, testes, and ovaries, but in none of these tissues were sig-

nificant trends in concentrations of cadmium found. Since rat prostate contains relatively high concentrations of zinc, repeated examination of the prostate for cadmium was carried out in order to ascertain whether cadmium replaced zinc *in vivo*, but no significant increase was found.

Tissue analyses of the control animals showed an increasing amount of cadmium in the tissues, but of very much lower amounts. It was eventually discovered that the M.R.C. rat diet 41 contained 5-10 μg. of cadmium per gram of food. This was later found to be due to the fish meal used to provide the protein in the diet. A sample of the latter supplied by the manufacturers of the diet was found to contain 160 μg. Cd/g. The small cadmium concentrations in the tissues of the control animals do not affect the results of the experiment since all the animals were fed on the same diet.

The growth curves of the experimental animals were of similar form to those of the control animals, but at a lower level. The female experimental animals had a final average weight of *c.* 220 g. compared with *c.* 245 g. for the controls, and the male experimental animals *c.* 240 g. compared with *c.* 370 g. for their controls. The weights illustrate that, as in the general condition of the animals observed during the experiment, the male rats were more severely affected than the females, despite their dosage at 0·75 mg./kg. for one month less than the females. No differences between the sexes were observed in tissue concentrations or histological findings at any stage of the experiment.

Discussion

The concentrations of cadmium in the livers and kidneys of the rats of experiment 3 were similar to those found in the post-mortem tissues of men who had been exposed to cadmium oxide fume, and the ratio of kidney concentration to that of the liver after dosage had been stopped followed a similar relationship but on a different time scale. The failure of other experimental workers, notably Princi and Geever (1950), to produce renal lesions in animals was probably due to their use of a lower dosage rate, which resulted in lower concentrations of cadmium in the liver and kidney than in the experiments now reported or in human post-mortem specimens. Thus the apparently high dosage rate of 0·75 mg./kg. thrice weekly is in fact one which the rats could tolerate to give tissue concentrations similar to those in workmen who received a lower dosage rate over a longer period.

The renal lesions resemble those of chronic pyelonephritis which is known to produce atrophy and distortion of tubules, increase of interstitial tissue, chronic inflammatory cell infiltration, and secondary ischaemic changes in the glomeruli.

Progressive tubular atrophy due to chronic infection, ischaemia, or cellular degeneration would be expected to produce lesions closely resembling one another with variations depending on the size of the obliterated blood vessels or the particular part of the tubules affected. Lymphocytes and occasional plasma cells may be associated with lesions without an infective cause, but infection is of course frequently associated with renal lesions of which the origin is obstructive or degenerative.

Tubular dilatation, mainly medullary, with increased amounts of interstitial tissue and mild inflammatory changes have been described as ageing changes in rats (Saxton and Kimball, 1941) and may add to the difficulty in interpreting experimental renal lesions but were not observed in the control animals in the experiments described in this paper.

The tubular cells are more likely to be subjected to a high concentration of some toxic substances than cells elsewhere in the body. Tubular atrophy from this cause or from interference with the normal metabolic processes of the cells may well prove to be responsible for certain examples of renal damage which are at present considered to be due to chronic pyelonephritis. An example of the difficulty in determining the origin of such renal lesions has arisen during the study of the effects of chronic potassium depletion on men and animals (Fourman, McCance, and Parker, 1956; Milne, Muehrcke, and Heard, 1957; Relman and Schwartz, 1958); minor cellular lesions are definitely associated with potassium depletion of short duration but chronic pyelonephritis has not yet been excluded as a cause of the chronic irreversible changes which have been observed. It is not possible to prove conclusively that the lesions described in this paper are not due to pyelonephritis occurring in sick rats but the evidence suggesting that they are the result of tubular atrophy due to cadmium poisoning is discussed below:

(1) The lesions observed in the kidneys of these animals differ in certain respects from those of chronic pyelonephritis. Chronic inflammatory cells although present were never as prominent as in pyelonephritis. The lesions were usually subcapsular in early cases and predominantly cortical in the later ones; the radial streaks of chronic inflammation, usually found in pyelonephritis, were not seen. Inflammatory changes beneath the pelvic epithelium were not found except in rats which had definite evidence of pyelonephritis with gross inflammatory lesions elsewhere in the renal parenchyma. "Thyroid" tissue, frequently found in chronic pyelonephritis, was not observed.

(2) If the lesions described had been produced by pyelonephritis acute focal inflammatory changes would have been expected to be frequently present in the kidneys of rats killed at about four months. These in fact were not found.

(3) The constant finding of excess red blood cells and casts in the urine of rats after four weeks in experiment 2 was not associated with any histological evidence of pyelonephritis when the rats were killed between six and nine weeks; the kidneys of two of these rats had no obvious histological abnormalities.

(4) The intensity of the renal damage appeared to be related to the dose of cadmium received. The lesions were more marked in the rats of experiment 2 which had received a total dose in 45 weeks of almost double the amount received by those in experiment 3 in 52 weeks.

(5) The appearance of early lesions after four months coincided with the attainment of a maximum cadmium concentration in the kidneys.

(6) No organisms were grown when cultures were made at 12 months from the kidneys of two control rats and three cadmium-injected rats with grade 3 histological lesions (one with polymorphonuclear leucocyte tubular casts). Two colonies of *E. coli* were, however, grown from the kidney of one cadmium-injected rat, which had grade 2 histological lesions and was killed at 12 months.

(7) The most advanced lesions were similar to those found in the kidneys of one man who died in uraemia, the result of chronic cadmium poisoning (Case A1, Bonnell, 1955). In his kidneys there was the same marked tubular atrophy but in addition there was pronounced subcapsular infiltration with chronic inflammatory cells and many glomeruli were transformed into fibrohyaline discs (Fig. 11).

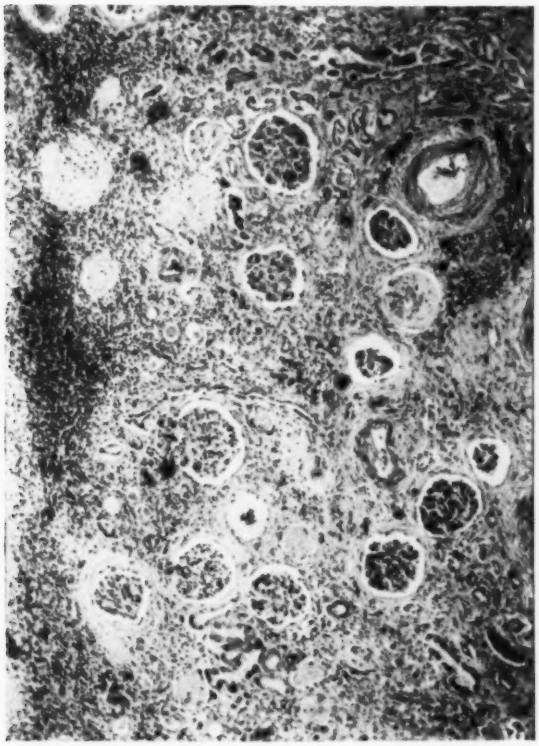


FIG. 11.—Male, aged 54 years. Haematoxylin and eosin, × 62. Cortex showing gross tubular atrophy, ischaemic and degenerative glomerular lesions, interstitial fibrosis, and marked subcapsular lymphocytic infiltration.

It is of interest that the tubular lesions in rats which were killed at 12 months, but which had not received injections after five and six months, were of comparable severity to those found in rats which had been injected with cadmium up to 12 months. The progression of the renal lesion after dosage had been stopped is of particular interest. It has been shown that in men the onset of cadmium proteinuria can occur many years after the last exposure to cadmium (Bonnell *et al.*, 1959). This suggests that a progressive toxic process may be present, eventually interfering with renal function, the first sign of which may not appear until many years after cessation of exposure. As with the rats in these experiments, the role of cadmium in relation to the progressive nature of the lesions is not clear. In the experimental animals there was a release of cadmium from the liver and this may have contributed to the production of the renal lesions, in addition to any damage caused by the cadmium already present in the kidneys.

The tissue concentrations of cadmium in liver and kidneys obtained at necropsy from five men who died of chronic cadmium poisoning are summarized in Table 2, together with years of exposure

TABLE 2

CADMIUM CONCENTRATION (μg./g.) OF LIVER AND KIDNEY FROM HUMAN CASES OF CHRONIC CADMIUM POISONING

Case No.	Years between Last Exposure and Death	Protein-uria	Renal Damage	Kidney (Cortex)	Liver
A1 (Bonnell, 1955)	2	+	+	62	330
B2 (Bonnell, 1955) (Smith *et al.*, 1957)	5	+	—	150	160
B6 (Bonnell, 1955)	5	—	—	360	300
Unpublished data (Bonnell)	10	—	—	170	65
B1 (Bonnell, 1955)	20	+	—	395	145

and the interval between last exposure and death. Other cases reported by Lane and Campbell (1954) and Friberg (1950a) are not in accordance with the above data. The concentrations of cadmium reported by them were of a different order of magnitude.

Stitch (1957) estimated spectrographically the cadmium content of tissues obtained at necropsies of people who died as the result of accidents and in whom there had been no occupational exposure to cadmium. The kidneys were found to contain the highest concentration of cadmium, suggesting that they selectively retain cadmium. It is possible that the concentration of cadmium in the kidneys following occupational exposure of men or experimental dosage of animals continues to increase until there is sufficient cadmium present in the renal parenchyma to cause damage. Certainly the concentration of cadmium in the kidneys remains at a high level both in men and in experimental animals (Figs. 7 and 9 and Table 2). This maintenance of renal cadmium levels is unlike the rapid fall of liver cadmium concentrations upon cessation of exposure, again demonstrable in both men and experimental animals.

We should like to thank Dr. Donald Hunter, Director of the Department for Research in Industrial Medicine, for his encouragement, and Professor Dorothy Russell for advice and for examining the kidneys of the animals in experiment 2, and also for permission to reproduce the photomicrograph of Fig. 11. We are indebted to Mr. B. T. Biles who carried out all the histological preparation and Mr. K. Baker who prepared and analysed the animal tissues for cadmium. We should also like to thank Mr. J. King for the photomicrographs and Dr. J. C. Smith for making available the tissue analyses of cases B1 and B6 in Table 2.

References

Alsberg, C. L., and Schwartze, E. W. (1919). *J. Pharmacol.*, **13**, 504.
Bonnell, J. A. (1955). *Brit. J. industr. Med.*, **12**, 181.
——, Kazantzis, G., and King, E. (1959). *Ibid.*, **16**, 135.
Dalhamn, T., and Friberg, L. (1957). *Acta path. microbiol. scand.*, **40**, 475.
Fourman, P., McCance, R. A., and Parker, R. A. (1956). *Brit. J. exp. Path.*, **37**, 40.
Friberg, L. (1948). *J. industr. Hyg.*, **30**, 32.
—— (1950a). *Acta med. scand., Suppl.* 240.
—— (1950b). *Arch. industr. Hyg.*, **1**, 458.
—— (1952). *A.M.A. Arch. industr. Hyg.*, **5**, 30.
Johns, C. O., Finks, A. J., and Alsberg, C. L. (1923). *J. Pharmacol.*, **21**, 59.
Lane, R. E., and Campbell, A. C. P. (1954). *Brit. J. industr. Med.*, **11**, 118.
Marmé, W. (1867). *Z. rationelle Med.*, **29**, 125.
Milne, M. D., Muehrcke, R. C., and Heard, B. E. (1957). *Brit. med. Bull.*, **13**, 15.
Princi, F., and Geever, E. F. (1950). *Arch. industr. Hyg.*, **1**, 651.
Prodan, L. (1932). *J. industr. Hyg.*, **14**, 174.
Relman, A. S., and Schwartz, W. B. (1958). *Amer. J. Med.*, **24**, 764.
Schwarz, L., and Otto, A. (1925). *Z. Hyg. Infekt.-Kr.*, **104**, 364.
Saxton, J. A., and Kimball, G. C. (1941). *Arch. Path. (Chicago)*, **32**, 951.
Severi, A. (1896). *Arch. Sci. med.*, **20**, 293.
Smith, J. C., Kench, J. E., and Smith, J. P. (1957). *Brit. J. industr. Med.*, **14**, 246.
Stitch, S. R. (1957). *Biochem. J.*, **67**, 97.
Wilson, R. H., DeEds, F., and Cox, A. J. (1941). *J. Pharmacol.*, **71**, 222.

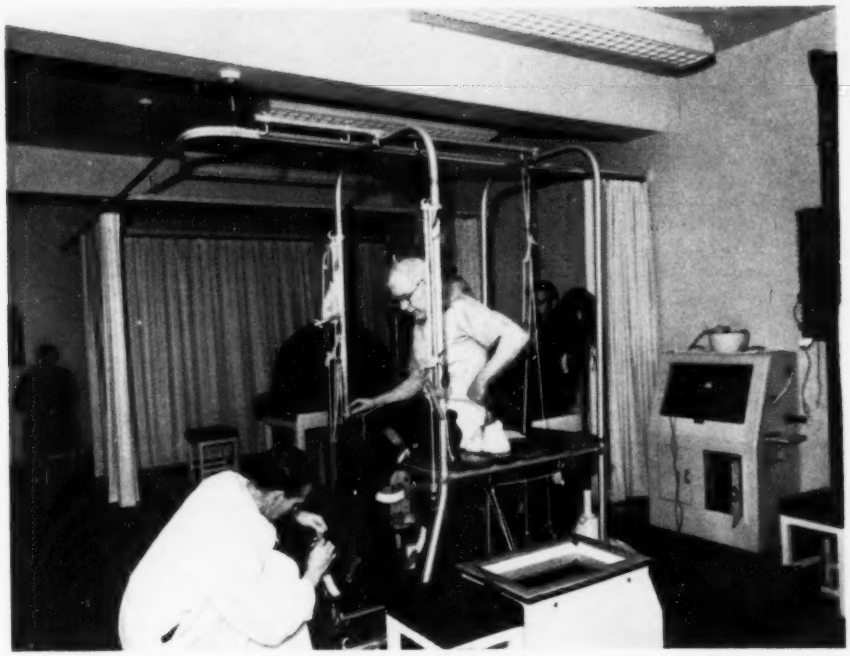


FIG.—The physiotherapy department at Elswick Works medical centre, showing the physiotherapist adjusting a remedial exercise apparatus to the needs of a patient.

Two New Medical Centres

New Medical Centres at Elswick Works, Newcastle-upon-Tyne

The new fully equipped centre provides for the care and treatment at work of the employees of Vickers-Armstrongs. The centre, staffed by a full-time medical officer, a sister in charge, and other fully trained people, is the final physical development of a medical "programme" begun in 1913 when the works corps of the St. John Ambulance Brigade was formed.

The centre is equipped for surgery, radiography, and physiotherapy. As well as routine medical examinations of new employees and of those beginning work again after an accident or illness, treatment is given at the centre to those requiring it so that time is not lost by the patient going elsewhere.

Those exposed to particular hazards, such as crane drivers and slingers, are given periodic medical examinations. Also, the medical staff are concerned to advise the management on problems of industrial hygiene and accident prevention. The employees too are taught the principles of accident prevention and health education generally.

New Medical Centre at Esso Refinery, Fawley

People working at the Esso Refinery, Fawley, now have a medical centre which is the hub of an intensive industrial health programme.

The building is beautifully planned and medically it is superbly equipped. Also it is charmingly decorated both for "out-patients" and "in-patients". There is a ward for patients, say, from tankers, requiring in-patient treatment for a short time.

The ambulance is particularly well equipped, every kind of accident at Fawley having been envisaged.

As in all works medical departments today, the stress is on preventive medicine as well as on treating day-to-day ills and accidents. To this end all employees are given a medical examination on joining, and those exposed to special hazards, *e.g.*, noise or lead, receive periodic medical examinations. Also, on a voluntary basis, a system of periodic check-ups for all employees has been started.

Training in first aid and safety is a natural part of the medical programme at a refinery, and this is so at Fawley. In addition courses, each of one week, in "emergency" medicine are given to tanker captains.

BOOK REVIEWS

The Handicapped and Their Rehabilitation. Edited by the late Harry A. Pattison; Introduction by Major General Melvin J. Maas. (Pp. xxxii + 944; illustrated. £5 12*s*. 6*d*.) Oxford: Blackwell Scientific Publications; Springfield, Illinois: Charles C. Thomas. 1957.

This book gives a comprehensive description of the rehabilitation services at present in operation in the U.S.A., together with some account of the extent of incapacity among the population at large. It is perhaps of interest to the lay administrator and those concerned with the ever widening field of rehabilitation activities rather than to members of the medical profession. Complete accounts are given of the practice in the Veterans Administration hospitals dealing with ex-service personnel and headed by a "physiatrist", a trained physician who correlates the activities of the various members of the rehabilitation team. This includes surgeon specialists, neurologists, psychiatrists, and specialists in all branches of medicine and surgery including the industrial doctor, as well as the ancillary services provided by the nurse, physiotherapist, dietician, social worker, clinical psychologist, vocational rehabilitation counsellor, and those concerned with recreation, religion, psycho-social welfare, and library services. Initial treatment is followed by educational and occupational therapy, progressing to vocational training (referred to as "manual arts therapy"), and special training for the blind, deaf, and aged. Experience in the Veterans Administration centres has shown that, as an investment, rehabilitation pays off economically. However, it appears that, from a practical point of view, with a few notable exceptions (the Liberty Mutual Insurance Company), rehabilitation of the injured worker is not provided for a large section of the community and too much reliance is placed on solving this problem on the medico-legal basis through compensation.

In some States, the cost and duration of medical treatment are limited by law, and in many others, the maximum weekly compensation is so low that the injured workman is forced to resume work before function and skill are completely recovered.

It is difficult to understand the inclusion of a chapter on plastic surgery in a book of this nature, but there is a good account of cardiovascular disease, including the appearance of death and disability claims under Workmens Compensation arising out of cardiovascular disease during the course of employment. The natural history of tuberculosis is dealt with in rather fuller detail than appears to be necessary and includes the remarkable statement that for every 100 marriages in the U.S.A. there are reported to be 30 or more divorces.

Awareness of the problem of the aged and what is being done for them is fully described, and a statistical review estimates that by 1960, 30% of the population of the United States will be between the ages of 40 and 65, and by 1976 some 80% of the 20 million people over 65 years of age will be eligible to draw a Federal pension.

The impact of industrial factors as a cause of deafness giving rise to compensable claims, has stimulated audiological research, and there are informative chapters on the rehabilitation of patients suffering from cancer, mental disease, epilepsy, and diabetes, the latter disease affecting about a million persons.

One learns that each year in the United States, some 90,000 workers are permanently disabled by industrial accidents and that, in contrast to what is being done for ex-service personnel under the Veterans Administration, it is only during recent years that individual States as well as a number of trade unions, have established their own rehabilitation and vocational training centres. A special course of training in "manual arts therapy" is now in existence, but a great deal more needs to be done in this direction through the medium of sheltered workshops providing employment for permanently incapacitated persons as exemplified by the Caterpillar Tractor Company. Federal legislation to provide for rehabilitation on a limited scale was first introduced in 1920 and was extended in 1943 under the exigencies of war. In 1954, the State Office of Vocational Rehabilitation was established under Public Law 565 of the Eighty-Third Congress in order to provide a full service on a national scale.

A. R. THOMPSON

Vore Almindelige Sygehuse og de Erhvervshaemmede (Need of Vocational Rehabilitation Among Patients Discharged from a Danish Hospital). By K. H. Backer. (Pp. vii + 306 pages with summary in English.) Copenhagen: Ejnar Munksgaard. 1958.

The purpose of this study was to ascertain to what extent patients admitted to the wards of general hospitals in Denmark during 1949 were discharged with a vocational problem due to a decrease in their working capacity, and what measures might be taken to prevent or remedy this state of affairs. Observations on 2,138 medical, surgical and gynaecological patients with an average age of 37·8 years and an average stay in hospital of 19·2 days, revealed the following: 81·1% were considered fit for work on discharge; 16·6% of the medical cases (about 50% of the whole) had reduced working capacity, of which 12·9% were considered in need of rehabilitation. Among the surgical cases, rehabilitation was considered to be necessary in 6·3%.

It is, therefore, recommended that the hospital staffs should pay more attention to this problem, particularly in long-term cases and cases of neuropsychosis, and that this need is just as real for all occupational groups as for the manual worker. There was evidence from the Disablement Insurance Court that rehabilitation may

have been started too late, and that there was lack of continuity in rehabilitation measures. The need is stressed for the creation of special rehabilitation and local vocational guidance centres which should work with, and not form part of, the hospitals.

A. R. THOMPSON

Pre-Employment Disability Evaluation. By William A. Kellogg; Preface by H. L. Herschensohn. (Pp. xv + 155. 80*s*.) Oxford: Blackwell Scientific Publications; Springfield, Illinois: Charles C. Thomas. 1957.

Pre-employment medical examination is less common in Great Britain than in the U.S.A. Under state compensation laws American employers can face financial loss if a man with some disability is given work for which he is not physically fit and where as a result he suffers further disablement. In such cases employers, with no national health service to fall back on, may be faced with the whole cost of medical treatment, sometimes extending over months or even years; large sums of money can thus be involved, apart entirely from compensation awarded by the courts.

The author of this book has examined medically in great detail some 20,000 applicants for employment in industry. His view is that examination must result in an accurate evaluation of disabilities. Disability must then be related to the man's working capacity, but no objective method is described by which this can be done. It is difficult, for example, to understand the reason for stating that " applicants for work as moulders and die finishers should have a red blood count and haemoglobin "; or that " applicants for key administrative positions should be rejected if their E.C.G., chest radiograph, or blood chemistry " varies " much from the normal ".

British readers will be interested to know that where there is no doctor available the American industrial nurse can be made responsible for pre-employment examinations. She can give decisions based on her findings. She may listen to the heart and lungs, and where the signs are " recognized " by her (whatever this may mean) she can reject an applicant. If she finds a positive Romberg test this "would be a cause for rejection", but no reason why is stated. The advice given to a nurse undertaking this work is: "When in doubt, reject".

In the author's experience " the mechanism of making certain that no one is assigned to the wrong type of activity can be controlled by the imposition [by the doctor] of appropriate restrictions ". Many of the restrictions listed seem reasonable in general terms but some of them are less realistic: " In plants where the noise registers 90 decibels or more the applicant should be prevented from working if he has a hearing loss of over 25% in one or both ears ". " Only applicants with minimal evidence of arthritic conditions should be approved for industrial work ". " Where there is doubt [in cardiac cases] the actual working capacity can only be ascertained through the test of actual performance on the job", but this reasonable advice is followed by a statement that in such cases " the advisable policy would be to reject such individuals and refer them to a rehabilitation agency for study and evaluation ".

It is our experience in this country that medical examinations before employment can be valuable where there is a proved hazard in the job and where a specified and generally agreed standard of physical fitness is required. So that advice can be accurate and effective the different demands of the job or range of jobs offered to an applicant for work should be made available to the doctor. There is wide variation in the reactions of individual persons to the physical and psychological demands of their occupation, and identical physical lesions may produce differing degrees of disablement. It is well known that many people with severe physical handicaps prove by satisfactory performance that they can contend on equal terms with their healthy fellow workers, for performance is not only related to physical capacity but depends also on attributes such as emotional stability, intelligence, and the response to incentives.

The type of medical examination suggested in the book is prodigious in extent. It must incur much of the doctor's time and be costly to the employer. In America this may be considered well worth-while, but if carried out in this country to any comparable extent it could well retard the development of a satisfactory industrial health service.

DONALD STEWART

Rehabilitation of the Hand. By C. B. Wynn Parry. (Pp. vii + 273 + Index; 101 figures. 45*s*.) London: Butterworth. 1958.

The hand is intolerant of disuse and the penalty is stiffness of the fingers. This principle must ever be remembered by those who treat its lesions and seldom has its application been better exemplified than at the R.A.F. Rehabilitation Centre at Chessington. This book records its practice.

Perhaps the best section is that on peripheral nerve injuries, though the chapters on the rheumatoid hand and on reconstructive hand surgery are admirable.

The use of lively splints, as one would expect, is rightly stressed and it should be possible for most occupational therapy departments to make them from the instructions given.

A few minor disagreements: early osteo-arthritis is surely one of the common causes of ulnar neuritis produced by lesions of the elbow. We have seldom seen adhesions of the extensor tendons following simple fractures of the metacarpals not caused by crush injuries properly treated, and fixation for three weeks is adequate for most simple metacarpal fractures.

The chapter dealing with resettlement inevitably makes the process look a little more cumbersome than it is. More stress might have been laid on the importance of the hospital surgeon getting in touch with the works doctor at an early date, thus preventing any resettlement problems arising—if the works is of any size. This chapter might well be reprinted as a leaflet and circulated to hospitals in industrial areas and to the teaching hospitals, especially the latter.

One intractable problem is the " compensation case ". Here we have to educate the legal profession or give judges medical assessors, when perhaps the scamp will cease to profit more from his injury than the honest man.

The book, which is handsomely produced, should be bought, read, and digested by all those who are responsible for the management of hand injuries and disabilities.

E. A. DEVENISH

Expert Committee on Medical Rehabilitation. First Report. [*Wld Hlh Org. techn. Rep. Ser. No. 158.*] (Pp. 52. 3*s.* 6*d.*) London: H.M.S.O.; Geneva: W.H.O. 1958.

The first session of the Expert Committee on Medical Rehabilitation was held in Geneva in the early part of 1958. The members of this Committee were Dr. F. S. Cooksey (England), Dr. G. Harlem (Oslo), Dr. H. H. Kessler (U.S.A.), Dr. M. Maurer (Rumania), Dr. E. Mindus (Sweden), Dr. F. E. de Godoy Moreira (Brazil), Professor J. Parisot (France), and Dr. R. Soeharso (Indonesia), together with representatives from the United Nations, the International Labour Organization, and the World Health Organization Secretariat.

Owing to the large field to be covered and the complexity of the subject, the Committee confined itself to discussing general principles and practices. It was agreed that medical rehabilitation was the fourth place in the whole scheme of health measures applicable to an individual or community, the others being promotion of health and prevention and treatment of disease: later on in their report, however, the point is made that good treatment includes all that is understood by rehabilitation and this is more in accord with present day ideas. As severely disabled people more frequently survive nowadays, due to advances in medical science, rehabilitation problems tend to increase and the many services concerned in the rehabilitation process demand good team work if success is to be attained. Some striking examples are given of how rehabilitation services have reduced the amount of invalidism in some countries and eased the burden of State payments to the disabled. The general aims and principles of rehabilitation are wisely defined but perhaps more stress might have been placed on the need of the patient himself cultivating a right attitude of mind towards recovery.

Particularly valuable sections of the report deal with the coordination of rehabilitation services and the education and training of medical and other persons working in this field. The expansion of the social services in recent years has greatly increased the doctor's responsibility and potential usefulness, and it is essential that medical students should fully understand this, and often have fuller instruction in the principles and practice of rehabilitation; there is also need of better postgraduate education in these matters. The report goes on to outline the help that relatives, employers, and fellow workers should give to those with disabilities, but rightly stresses the doctor's duty to be well informed of rehabilitation techniques, to teach, and to lead the rehabilitation team.

In some appendices to their report the authors discuss the psychological aspects of rehabilitation, rehabilitation in some less developed countries and some special problems of the blind, deaf, and chronically ill, and end with some recommendations for further study and action. They consider that while the techniques for rehabilitating those with orthopaedic and special senses handicaps have been well developed, more attention should now be paid to medical disabilities such as those due to circulatory, respiratory, and digestive disorders. They urge that thought should be given by the appropriate international organizations to the meaning of words such as "disability" and "impairment" and agreement sought regarding terminology. The extent of the rehabilitation problem should be studied by means of field surveys in individual countries, and where social security systems have been well developed these should be better coordinated with the machinery of rehabilitation. Good collaboration between government departments dealing with this subject on a national level is advocated, and the need is stressed of suitable training for all persons concerned in this work.

T. G. FAULKNER HUDSON

Ageing and Human Skill. By A. T. Welford. (Pp. viii + 300; illustrated. 25*s.*) Published for the Nuffield Foundation by Oxford University Press, London. 1958.

This book is an account of the research carried out by the Nuffield Unit for Research into Problems of Ageing from 1946 to 1956. It extends and deepens the pioneer work on human performance started by Bartlett and Craik during the last war. Perhaps a better title would have been "Ageing and Performance" because the research has covered a much wider field than that customarily denoted by the term "skill". Perception, problem solving, memory, adaptability, as well as motor skill, are some of the areas in which studies have been carried out.

The bulk of the work is experimental and the experiments are distinguished by the ingenuity with which they have been designed to examine fundamental problems but, at the same time, to preserve some analogy to tasks met outside the laboratory. The strategy of research may be taken as a model of what research should be. Rather general questions are asked first of all and then more precise information is gained by the use of additional controls. Although the investigations explore very different aspects of behaviour, they are unified through their interpretation by information theory concepts. The explanatory power and fruitfulness of this approach to psychological phenomena cannot be fully appreciated until the attempt is made to account for some of the more interesting findings in terms of stimulus-response learning theory.

The author's main conclusion is that changes in performance with age are due not so much to impairment in receptor and effector organs as to failure of central mechanisms to guide and control appropriate action. This failure is discussed in terms of "diminished channel capacity", "lowering of signal to noise ratio", and "lessened short-term storage of information". It is further suggested that the organic correlate of this failure may be found in the decrease in the number of active brain cells associated with increasing age. However, evidence is also adduced to show that older people compensate to some extent by an automatic adjustment of their activity to a level appropriate to their capacity.

The presentation strikes a reasonable balance between the detailed research paper and the semi-popular and inevitably over-simplified summary of results. And this should make the book suitable for industrial medical

officers and personnel managers who are seriously interested in the problems of performance and ageing. But it is not easy reading. In particular, the rather abstract chapter entitled, "On the Nature of Skill", although a masterpiece of condensation, may be unenlightening to those not conversant with contemporary psychology. (On the other hand it should be compulsory reading for third year psychology undergraduates.) In conclusion, it may be said that if someone wished to know what kind of sustained research had been done by experimental psychologists in this country since the war, no better examples could be found for them than the investigations reported here.

P. C. WASON

Een Onderzoek naar de asthmatische aard der Borstklachten van de Arbeiders in de Steenkolenmijnen (The Role of Asthmatic Predisposition in Coal Miners' Chest Complaints). By K. de Vries. (Pp. v + 124; 7 figures, 30 tables, 217 references. No price given.) Groningen: J. B. Wolters. 1958.

It has become increasingly obvious that in anthraco-silicosis (coalworkers' pneumoconiosis) there is no close relationship between the severity of respiratory symptoms and the radiological changes in the lungs. The ingenious study described in this thesis was undertaken in order to investigate the hypothesis that miners' chest complaints are influenced by an asthmatic predisposition. An earlier survey of school children living in a mining community enabled the author to sample children with asthma and asthma-free controls, matched for age, sex, and place of residence. The male mining relatives of these two groups, 260 in the asthma and 104 in the control group, were then compared using the information given on the health record cards available for each man. (It should be noted that the meaning of the term "asthma" used in this work is wider than that now current in this country and includes what we should call chronic bronchitis and emphysema.)

The ages of the two groups were similar; but the occupational histories differed, the proportion of miners working underground being lower in the asthma group, a finding the author attributes to self-selection. The number of days of disability due to dyspnoea, wheezing, chest pain, and cough was higher in the asthma group than in the controls and also in those working underground compared with those on the surface. Periodic radiographs of the chest of every miner have been taken since 1949. No significant difference in the prevalence of anthraco-silicosis was observed between asthma and control groups, but among the young miners in the asthma group a significantly higher proportion of non-anthraco-silicotic lesions of the lower lung field, costophrenic sinus, and diaphragm was observed.

The author concludes that his findings support the hypothesis. He considers that they also indicate that miners' chest complaints are influenced by the underground milieu but not by the degree of anthraco-silicosis.

A detailed English summary and English subtitles to the tables and diagrams enable those who do not read Dutch to understand the greater part of this interesting monograph, which includes a very complete review of the literature.

I. T. T. HIGGINS

Occupational Allergy. Lectures held during a course on occupational allergy organized under the auspices of the European Academy of Allergy; Foreword by D. A. Williams. (Pp. xvi + 329; illustrated. Fl. 30.-.) Leiden, Holland: H. E. Stenfert Kroese N.V. 1958.

This book consists of 38 lectures given in May, 1958, under the auspices of the European Academy of Allergy. It is concerned with allergic reactions affecting the skin, eyes, and respiratory tract. The occupational aspects are broadly treated, since consideration is given both to those workers with pre-existing allergic manifestations and to the sensitization effects induced by working conditions; these are treated in some instances by industrial groups (bakers, pharmaceutical workers, printers, mine workers, cigar makers, cotton printers, and even the medical profession and its auxilaries), in others by discussion of offending substances (kapok, wool, turpentine, formaldehyde, wood dust, coffee, and pencillin). Other lectures discuss the diagnosis of allergic diseases and delimitation of their occupational aspects, some consideration of the mechanism of sensitization, therapy, prevention, and compensation. A useful contribution from Dr. D. A. Williams evaluates statistically the "social consequences" of asthma, urticaria, other allergic disorders, eczema, and dermatitis; this work is based on the reports of our Ministry of Pensions and National Insurance, and it is probably true to say that comparable information hardly exists for other parts of the world.

The merits of this book grow out of its broad scope, its widely European authorship, and the speed of publication. Its weaknesses mainly stem from the same origins. The lectures are uneven in quality and include much that is already well known. They overlap considerably, and some contain large numbers of spelling mistakes and printers' errors. Some include details of the author's place of work and country of origin, others leave the reader to guess. Some give properly set out lists of references, others mention authors (with dates) in the text, but give no other help to those who would like to consult the original source. The chapters which stand out as specially good concern nasal affections as occupational diseases and occupational sensitization of the air passages by organic dust; there are also stimulating discussions of turpentine and of the dyes used in cotton printing.

J. R. SQUIRE

Noise and Your Ear: Modern Monographs in Industrial Medicine. 1. By Aram Glorig, Jr. (Pp. viii + 152; illustrated. 46*s*.) New York and London: Grune & Stratton. 1958.

Acoustics, Noise, aud Buildings. By P. H. Parkin and W. R. Humphreys. (Pp. 331; illustrated. 70*s*.) London: Faber and Faber. 1958.

Here are two recent additions to the current flood tide of literature concerning noise. They arrive at a time when British industry and industrial physicians are taking a much closer interest in this particular aspect of the physical environment, and at a time when for many of us life is on the verge of becoming even noisier. Although each is written for a different public each, in its own way, is authoritative.

Glorig's small but expensive monograph (over three shillings per page!) can immediately be assessed as well worth the cost. It is the first of a series of modern monographs in industrial medicine, the whole series to be edited by A. J. Lanza; future projects concern industrial rehabilitation, alcoholics at work, sight conservation, and the employment of cardiac patients. If these promised siblings all prove to be as readable and explicit as their "noisy" elder brother, Dr. Lanza will have fathered a family of notable distinction.

The monograph is written "primarily for persons who require only a general knowledge of the subject, persons who are interested in many biologic hazards of which noise exposure is only one, and persons who may find it their responsibility to organize noise control programmes and hearing conservation programmes".

The author writes with acknowledged authority. He is Director of Research, Sub-Committee on Noise in Industry of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology.

The book is divided into seven sections: Introduction; The Ear and Hearing; Audiometry; Hearing Loss; Effects of Noise Exposure; Conservation of Hearing; and Compensation and Rating Scales. This may not necessarily be a logical sequence but the text and the development of concepts flow smoothly.

The glossary of audiological terms in section I.3 is particularly useful. Herein the author emphasizes (p. 21) the importance of identifying the reference level whenever sound levels are quoted. This he himself assiduously does, except on p. 50, Fig. 5, 4, where the reference level of the ordinate expressed in decibels is omitted but understood to be 0·0002 dynes per square centimetre. This, however, is but a trivial omission.

In 9.5 (pp. 83 and 84) which deals with the proper care and calibration of audiometers, mention is not made of the British standard of calibration which differs significantly from its transatlantic counterpart. As the monograph is published both in New York and London this can be misleading for British readers. The somewhat parochial attitude in relation to statutory recognition of occupational hearing loss is surprising in a book presumably designed for international reference. Some 20 countries have specific legislation of this nature (Great Britain is not amongst them) and "blanket coverage" for all forms of ills occupationally arising is a feature of many lands. The question raised therefore is not carping by a "little englander": many large international consortia and transport organizations operate hazardously noisy processes in countries having an explicit legal remedy for locally employed nationals.

Some authorities in this country might not readily accept the author's estimate (p. 133) of noise-induced hearing loss in the industrial population, based on the 1954 Wisconsin State fair hearing survey; statistical objections, in part valid, can be postulated. The estimated possible cost of compensation in the United States during the next decade is quoted as 154 million dollars if the specific criteria pertaining in the State of Wisconsin are applied; such talk of Eldorado makes the humblest physician here feel quite heady!

The discussion of compensation and rating scales is particularly interesting for readers here; a great deal can be learned from such transatlantic experience.

"Acoustics Noise and Buildings" is produced by a scientist from the Building Research Station (Parkin) and a consultant architect (Humphreys), in a more simple and comprehensible manner than Harris', "Handbook of Noise Control" and it covers many aspects therein considered. The book will be of particular interest to the architect, the acoustics engineer, and all who are interested in achieving at the design stage, conditions likely to augment working efficiency. The main emphasis is on criteria of acoustic comfort rather than on safety for noise-induced hearing loss.

The chapters dealing with the nature of sound, behaviour of sound in rooms, sound insulation and noise control, and that on criteria for sound insulation and noise control, possess interest for readers of this journal. Appendix A contains a useful table of absorption coefficients of some 65 materials commonly used in sound insulation planning. Appendix D tables a baker's dozen of some everyday industrial noises analysed in octave bands. Few industrial physicians would need to have this book always to hand, but it is a valuable reference source when considering architectural plans for noisy sites, or for premises where the exacting and skilled nature of the job demands freedom from distracting sound.

OWEN MCGIRR

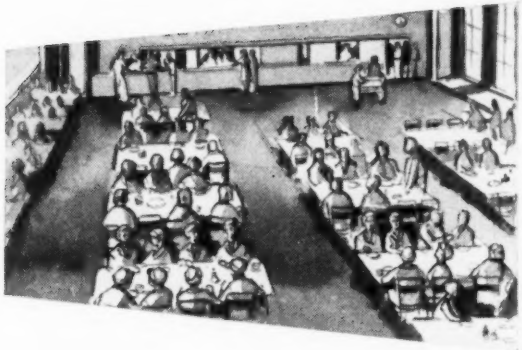
Recent Studies in Epidemiology. Edited by J. Pemberton and H. Willard. (Pp. xiii + 203; illustrated. 25*s*.) Oxford: Blackwell Scientific Publications. 1958.

The 18 papers in this book were presented at the Study Group on Current Epidemiological Research organized by the International Corresponding Club and held in Holland in 1957. The aim, which has been realized, was to assemble information on the ways in which epidemiological methods are being used in different parts of the world to investigate the incidence and causation of disease and to assess the needs of communities for various health services. The main topics discussed and covered by the chapters of the book are: the use of existing morbidity and the mortality records in epidemiological research; the *ad hoc* field survey or getting your own data; the evaluation of health needs and services by the epidemiological method including applications to underdeveloped territories; application of the epidemiological method to problems in mental health; general practice as a field for epidemiology.

This is not a text-book of epidemiology; it goes further than a text-book in giving practical examples, carefully worked out by experts, of epidemiological techniques. These examples will be of great help to those who wish to brush up their epidemiology. Some, such as the studies of sickness absence records in chronic bronchitis (D. D. Reid), observer error (C. M. Fletcher), and cancer of the lung and cancer of the nose in nickel refiners (W. Richard Doll), are of direct interest in occupational health.

L. G. NORMAN

Where Coughs are a Danger



Loss of labour and production resulting from infections spread by cough, can be greatly reduced by treatment of coughs with 'Phensedyl'.

Pleasant tasting 'Phensedyl' is a well balanced combination with antitussive, local analgesic and antihistamine properties. It gives rapid relief in all types of cough.

'Phensedyl'

trade mark *brand*

PROMETHAZINE COUGH LINCTUS

An **M&B** *brand Medical Product*

MANUFACTURED BY

MAY & BAKER LTD

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

Tel: DOMinion 3060, Ext. 266 and 267

MA6792

Glorig's small but expensive monograph (over three shillings per page!) can immediately be assessed as well worth the cost. It is the first of a series of modern monographs in industrial medicine, the whole series to be edited by A. J. Lanza; future projects concern industrial rehabilitation, alcoholics at work, sight conservation, and the employment of cardiac patients. If these promised siblings all prove to be as readable and explicit as their "noisy" elder brother, Dr. Lanza will have fathered a family of notable distinction.

The monograph is written "primarily for persons who require only a general knowledge of the subject, persons who are interested in many biologic hazards of which noise exposure is only one, and persons who may find it their responsibility to organize noise control programmes and hearing conservation programmes".

The author writes with acknowledged authority. He is Director of Research, Sub-Committee on Noise in Industry of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology.

The book is divided into seven sections: Introduction; The Ear and Hearing; Audiometry; Hearing Loss; Effects of Noise Exposure; Conservation of Hearing; and Compensation and Rating Scales. This may not necessarily be a logical sequence but the text and the development of concepts flow smoothly.

The glossary of audiological terms in section 1.3 is particularly useful. Herein the author emphasizes (p. 21) the importance of identifying the reference level whenever sound levels are quoted. This he himself assiduously does, except on p. 50, Fig. 5, 4, where the reference level of the ordinate expressed in decibels is omitted but understood to be 0·0002 dynes per square centimetre. This, however, is but a trivial omission.

In 9.5 (pp. 83 and 84) which deals with the proper care and calibration of audiometers, mention is not made of the British standard of calibration which differs significantly from its transatlantic counterpart. As the monograph is published both in New York and London this can be misleading for British readers. The somewhat parochial attitude in relation to statutory recognition of occupational hearing loss is surprising in a book presumably designed for international reference. Some 20 countries have specific legislation of this nature (Great Britain is not amongst them) and "blanket coverage" for all forms of ills occupationally arising is a feature of many lands. The question raised therefore is not carping by a "little englander": many large international consortia and transport organizations operate hazardously noisy processes in countries having an explicit legal remedy for locally employed nationals.

Some authorities in this country might not readily accept the author's estimate (p. 133) of noise-induced hearing loss in the industrial population, based on the 1954 Wisconsin State fair hearing survey; statistical objections, in part valid, can be postulated. The estimated possible cost of compensation in the United States during the next decade is quoted as 154 million dollars if the specific criteria pertaining in the State of Wisconsin are applied; such talk of Eldorado makes the humblest physician here feel quite heady!

The discussion of compensation and rating scales is particularly interesting for readers here; a great deal can be learned from such transatlantic experience.

"Acoustics Noise and Buildings" is produced by a scientist from the Building Research Station (Parkin) and a consultant architect (Humphreys), in a more simple and comprehensible manner than Harris', "Handbook of Noise Control" and it covers many aspects therein considered. The book will be of particular interest to the architect, the acoustics engineer, and all who are interested in achieving at the design stage, conditions likely to augment working efficiency. The main emphasis is on criteria of acoustic comfort rather than on safety for noise-induced hearing loss.

The chapters dealing with the nature of sound, behaviour of sound in rooms, sound insulation and noise control, and that on criteria for sound insulation and noise control, possess interest for readers of this journal. Appendix A contains a useful table of absorption coefficients of some 65 materials commonly used in sound insulation planning. Appendix D tables a baker's dozen of some everyday industrial noises analysed in octave bands. Few industrial physicians would need to have this book always to hand, but it is a valuable reference source when considering architectural plans for noisy sites, or for premises where the exacting and skilled nature of the job demands freedom from distracting sound.

OWEN MCGIRR

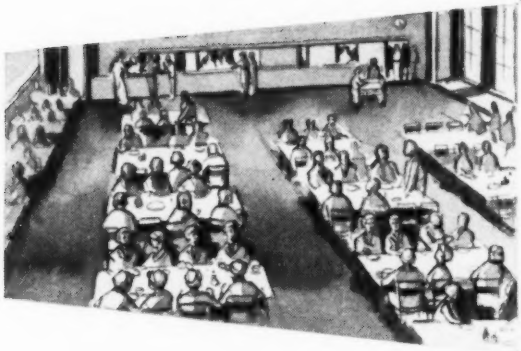
Recent Studies in Epidemiology. Edited by J. Pemberton and H. Willard. (Pp. xiii + 203; illustrated. 25*s*.) Oxford: Blackwell Scientific Publications. 1958.

The 18 papers in this book were presented at the Study Group on Current Epidemiological Research organized by the International Corresponding Club and held in Holland in 1957. The aim, which has been realized, was to assemble information on the ways in which epidemiological methods are being used in different parts of the world to investigate the incidence and causation of disease and to assess the needs of communities for various health services. The main topics discussed and covered by the chapters of the book are: the use of existing morbidity and the mortality records in epidemiological research; the *ad hoc* field survey or getting your own data; the evaluation of health needs and services by the epidemiological method including applications to underdeveloped territories; application of the epidemiological method to problems in mental health; general practice as a field for epidemiology.

This is not a text-book of epidemiology; it goes further than a text-book in giving practical examples, carefully worked out by experts, of epidemiological techniques. These examples will be of great help to those who wish to brush up their epidemiology. Some, such as the studies of sickness absence records in chronic bronchitis (D. D. Reid), observer error (C. M. Fletcher), and cancer of the lung and cancer of the nose in nickel refiners (W. Richard Doll), are of direct interest in occupational health.

L. G. NORMAN

Where Coughs are a Danger



Loss of labour and production resulting from infections spread by cough, can be greatly reduced by treatment of coughs with 'Phensedyl'.

Pleasant tasting 'Phensedyl' is a well balanced combination with antitussive, local analgesic and antihistamine properties. It gives rapid relief in all types of cough.

'Phensedyl'

trade mark *brand*

PROMETHAZINE COUGH LINCTUS

An **M&B** *brand Medical Product*

MANUFACTURED BY

MAY & BAKER LTD

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

Tel: DOMinion 3060, Ext. 266 and 267

MA6792

Don't waste man hours -it's costly!

X-Ray Unit in position ready to commence examinations

Please write stating your requirements for quotation or ask our representative to call.

To keep the 'Queen of the Seas' in dock is a costly business. That is why Portable X-Rays were chosen by the London Hospital Department for Research in Industrial Medicine (Medical Research Council) to assist in a special investigation into the health of the Boiler Scalers on the 'Queen Mary'.

Mobile X-Ray Units of Portable X-Rays Ltd. are regularly employed by large industrial organisations for chest examinations on site during working hours with economy in time and money.

PORTABLE X-RAYS LIMITED

POWER ROAD, CHISWICK, LONDON, W.4. *Tel. : CHIswick 7836/7*

* **A significant reduction in healing time for**

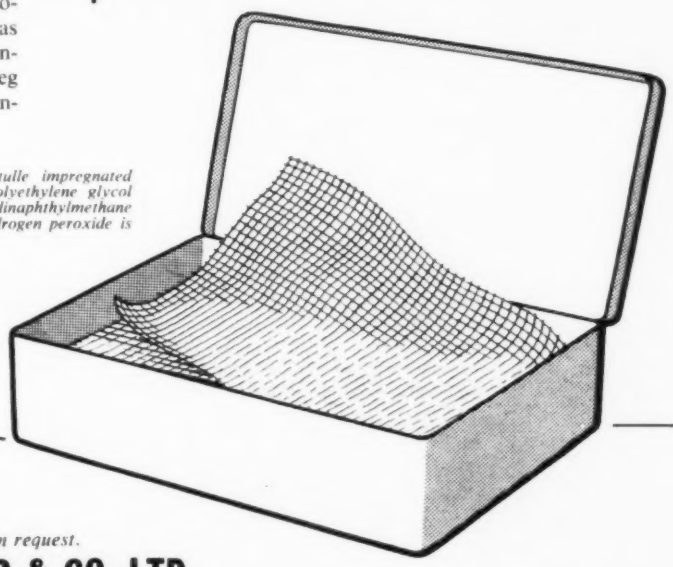
BURNS

VIACUTAN

tulle

* In a recent clinical trial in a casualty department, 75 cases of burns treated with this dressing healed significantly more rapidly than a control series of 75 cases treated with ordinary paraffin tulle. (Brit. J. Plastic Surgery, October 1959, **12**, 238). Viacutan Tulle has shown similar advantages over conventional dressings in cases of leg ulceration, pressure sores and unstitched lacerations.

1 Does not stick fast to the lesion.
2 Dries up exudate.
3 Eliminates infection.



The dressing consists of cotton tulle impregnated with a water-soluble, non-greasy polyethylene glycol mass, and containing silver dinaphthylmethane disulphonate (Viacutan). Urea hydrogen peroxide is added as an oxidizing agent.

Packed in boxes of 50 pieces

A WB MEDICAL PRODUCT

Further information and samples on request.

WARD, BLENKINSOP & CO. LTD.

37 QUEEN SQUARE, W.C.1

Telephone: HOLborn 5992/6 (5 lines). Telegrams: Duochem, Westcent, London.

I.C.I. designed this barrier cream specially for industry

Extensively used in I.C.I.'s own factories,
I.C.I. Barrier Cream
gives better skin protection

* Gives equal protection in wet or dry work.
* Safeguards against industrial dermatitis.
* Protects the hands from staining and ingrained dirt.
* Hands come clean more easily after work.

In containers of 5 lb.

For further information and literature, please write to your nearest I.C.I. Sales Office, or direct to Wilmslow.

I.C.I. BARRIER CREAM

Special rates for bulk contracts

IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

ICI

Ph. 914

DIPLOMA IN INDUSTRIAL HEALTH *of the* SOCIETY OF APOTHECARIES OF LONDON

The Society of Apothecaries of London, conscious of the paramount importance of an efficient health service in Industry, has instituted this Diploma in Industrial Health, which is of a very high standard and is open to registered medical practitioners, members of H.M. Services, and others, such as Examining Surgeons, etc.

The Examination—which consists of three Papers, Oral and Clinical — is held in July and December.

The next Examination begins on July 11th, 1960.

Regulations and Forms of Application for Admission to the Examinations may be obtained from

The Registrar,

SOCIETY OF APOTHECARIES OF LONDON

BLACK FRIARS LANE, E.C.4

Is the incidence of Dermatitis in Industry declining?

No! The Annual Report of the Chief Inspector of Factories indicates that dermatitis in industry is not lessening. Yet the incidence can be controlled by using the appropriate Rozalex Barrier Cream for the work involved. These barrier creams have been accepted as the standard preparations for over 25 years by those concerned with occupational health. The severity of the risk varies with the trade, but in all occupations there is need for protection and cleanliness. Full technical resources are available on request to Rozalex Limited, 10 Norfolk Street, Manchester 2.

Protect hands with

ROZALEX BARRIER CREAMS

R111A

Not this....

Personnel should be urged never to neglect minor cuts or abrasions. Immediate attendance at the first aid centre can avoid the secondary infection that so frequently leads to lost time. Among canteen staff particularly, immediate dressing of small wounds is vital, to prevent ingress and egress of infective organisms.

but this!

DALMAS FIRST AID

Samples and literature from
DALMAS LTD. Dept. Junior Street, LEICESTER

'MORE CORN FROM FINSBURY SQUARE?

"Now, now . . . a little more respect from you, my lad — that was one of the old masters of our early advertising (Hassell, circa 1912).

And what's more, we're still first past the post with our products . . . Sternocleanse Barrier Cream always wins hands down!"

STERNOL

STERNOCLEANSE BARRIER CREAM

STERNOL LTD., ROYAL LONDON HOUSE, FINSBURY SQUARE, LONDON E.C.2. TELEPHONE: MONarch 3871-5

INDUSTRIAL CLEANLINESS

SAROUL gives 24 hour protection to hands & skin

Adequate protection is ensured by using Saroul after work—it is scientifically compounded to remove grime and dirt quickly and completely. It is not a harsh antiseptic but a cleansing agent which assists the natural healing processes and extends its protective effect for many hours. Saroul is a positive safeguard against industrial dermatitis.

Testing samples and literature free on request to Dept. BS.

SAROUL Antiseptic Hand Cleanser is made by

Sandeman Brothers Ltd.

BILSLAND DRIVE · MARYHILL · GLASGOW

SPECIALIST JOURNALS

ANNALS OF THE RHEUMATIC DISEASES
Quarterly. Annual Subscription, £3.

ARCHIVES OF DISEASE IN CHILDHOOD
Bi-monthly. Annual Subscription, £4 4s

BRITISH HEART JOURNAL
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF INDUSTRIAL MEDICINE
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF PHARMACOLOGY AND CHEMOTHERAPY
Quarterly. Annual Subscription, £4 4s

BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF VENEREAL DISEASES
Quarterly. Annual Subscription, £3.

JOURNAL OF CLINICAL PATHOLOGY
Bi-monthly. Annual Subscription, £4 4s

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY
Quarterly. Annual Subscription, £3.

MEDICAL AND BIOLOGICAL ILLUSTRATION
Quarterly. Annual Subscription, £3.

THORAX
Quarterly. Annual Subscription, £3.

BRITISH JOURNAL OF OPHTHALMOLOGY
Monthly. Annual Subscription, £6.

OPHTHALMIC LITERATURE
Six issues and index yearly. Annual Subscription £4 4s
Combined subscription with British Journal of Ophthalmology, £9

BRITISH MEDICAL ASSOCIATION
B.M.A. House, Tavistock Square, London, W.C.1

DILACOL reduces absenteeism from the common cold

DILACOL *"the drug of choice for use in large industrial concerns, or closed communities, in an attempt to reduce the spread of acute coryza"*

Scot. med. J., 1958, 4, 199

DILACOL makes colds shorter

DILACOL helps to prevent secondary infection following a cold

DILACOL makes colds easier to bear, and keeps people at work without impairment of efficiency or initiative

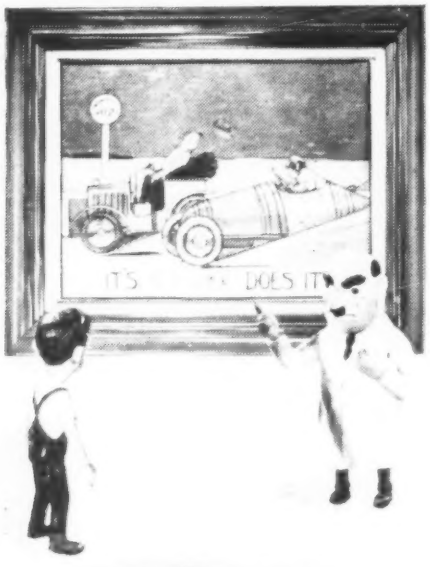
The conclusion quoted above was reached by the author after a 2-years trial. The outstanding result was that 76% of Dilacol-treated patients had NO symptoms after 4 days treatment, while only 8% of placebo-treated patients were symptom-free.

Dilacol contains 1.5 mg. Perdilatal, a vasodilator; 50 mg. quinine HCl; and 60 mg. propyl salicylamide. By increasing blood flow in the nasal mucosa in the early stages of a cold, it helps to prevent the catarrhal and mucopurulent stages, relieves symptoms and promotes a feeling of well-being. The course of the cold is shortened.

Detailed information on the use of Dilacol in industrial concerns is available on request. So are samples.

Smith & Nephew *Pharmaceuticals* Limited

WELWYN GARDEN CITY, HERTFORDSHIRE



'MORE CORN FROM FINSBURY SQUARE?

"Now, now . . . a little more respect from you, my lad — that was one of the old masters of our early advertising, Hassell, circa 1912 . . . And what's more, we're still first past the post with our products . . . Sternocleanse Barrier Cream always wins hands down!"

STERNOL

STERNOCLEANSE BARRIER CREAM

STERNOL LTD., ROYAL LONDON HOUSE, FINSBURY SQUARE, LONDON E.C.2. TELEPHONE: MONarch 3871-5

INDUSTRIAL CLEANLINESS

SAROUL gives 24 hour protection to hands & skin

Adequate protection is ensured by using Saroul after work—it is scientifically compounded to remove grime and dirt quickly and completely. It is not a harsh antiseptic but a cleansing agent which assists the natural healing processes and extends its protective effect for many hours. Saroul is a positive safeguard against industrial dermatitis.

Testing samples and literature free on request to Dept. BS

SAROUL Antiseptic Hand Cleanser is made by

Sandeman Brothers Ltd.

BILSLAND DRIVE MARYHILL GLASGOW

SPECIALIST JOURNALS

ANNALS OF THE RHEUMATIC DISEASES

ARCHIVES OF DISEASE IN CHILDHOOD

BRITISH HEART JOURNAL

BRITISH JOURNAL OF INDUSTRIAL MEDICINE

BRITISH JOURNAL OF PHARMACOLOGY AND CHEMOTHERAPY

BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE

BRITISH JOURNAL OF VENEREAL DISEASES

JOURNAL OF CLINICAL PATHOLOGY

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY

MEDICAL AND BIOLOGICAL ILLUSTRATION

THORAX

BRITISH JOURNAL OF OPHTHALMOLOGY

OPHTHALMIC LITERATURE

BRITISH MEDICAL ASSOCIATION

B.M.A. House, Tavistock Square, London, W.C.1

DILACOL reduces absenteeism from the common cold

DILACOL *"the drug of choice for use in large industrial concerns, or closed communities, in an attempt to reduce the spread of acute coryza"*

Scot. med. J., 1959, 4, 199

DILACOL makes colds shorter

DILACOL helps to prevent secondary infection following a cold

DILACOL makes colds easier to bear, and keeps people at work without impairment of efficiency or initiative

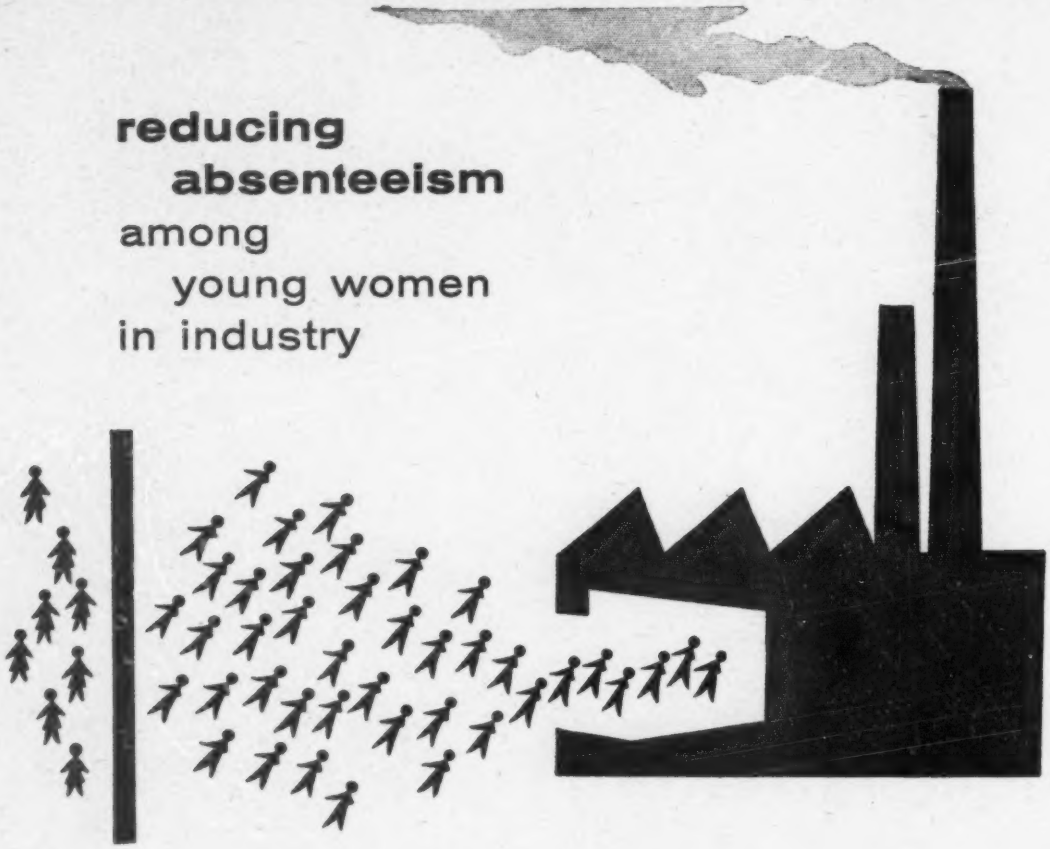
The conclusion quoted above was reached by the author after a 2-years trial. The outstanding result was that 76% of Dilacol-treated patients had NO symptoms after 4 days treatment, while only 8% of placebo-treated patients were symptom-free.

Dilacol contains 1.5 mg. Perdilatal, a vasodilator; 50 mg. quinine HCl; and 60 mg. propyl salicylamide. By increasing blood flow in the nasal mucosa in the early stages of a cold, it helps to prevent the catarrhal and mucopurulent stages, relieves symptoms and promotes a feeling of well-being. The course of the cold is shortened.

Detailed information on the use of Dilacol in industrial concerns is available on request. So are samples.

Smith & Nephew
***Pharmaceuticals* Limited**
WELWYN GARDEN CITY, HERTFORDSHIRE

reducing absenteeism among young women in industry



The fact that spasmodic dysmenorrhoea ranks as an important socio-economic problem[1] will not surprise the Industrial Medical Officer. Neither will the incidence of absenteeism — regarded as routine by many sufferers.[1] Buscopan presents the Industrial Medical Officer with an original and highly effective treatment for this condition. A treatment, moreover which allows the patient to remain at her employment without discomfort and with her faculties unimpaired. Buscopan is *not* symptomatic treatment, it is a rational, specific therapy. It is, in fact, the only drug of its type that acts directly on the parasympathetic innervation of the uterus, relieving spasm of the uterine muscle swiftly and with a virtual absence of side-effects. Buscopan is excellently tolerated, has no effect on the higher centres and alleviates the condition of spasmodic dysmenorrhoea smoothly and quickly.

1 (1957) *Practitioner* 178, 320

BUSCOPAN*

Hyoscine-N-Butylbromide

for spasmodic dysmenorrhoea

Manufactured and distributed in the U.K. by Pfizer Ltd., Folkestone, Kent for

C. H. BOEHRINGER SOHN, INGELHEIM am RHEIN

Registered proprietors of the Trade Mark. *Regd. Trade Mark.

PRINTED IN ENGLAND BY THE THANET PRESS, MARGATE